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National Institutes of Health
1968
annual report

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
U.S. National Institutes of Health
" Bethesda, Md. 20014

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PREFACE

The National Institutes of Health, principal agency of the Federal government responsible for biomedical research, communication of biomedical knowledge, and education for the health professions, reports yearly to the public on its activities. This account always forms a part of a larger document, the Annual Report of the Department of Health, Educaton, and Welfare.

Fiscal Year 1968 was a particularly active one for the National Institutes of Health, characterized by substantial changes in organization, broadening scope of operation, and fruitful application of resources. To permit full dissemination of information on its responsibilities and accomplishments to those with particular interest in NIH, the 1968 Annual Report is reprinted separately in this volume. Appropriate tables are appended to show appropriations, grants and other extramural awards, and personnel levels.

It is hoped this publication will serve as a ready reference source both for those concerned with the new responsibilities and those interested in problems encountered and results achieved in traditional NIH endeavors.

Robert Q. Marston, M.D.

Robert Q. Marston, M.D.
Director

Officers
NATIONAL INSTITUTES OF HEALTH
as of
September 1, 1968

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G. Donald Whedon, M.D.	*Director, National Institute of Arthritis and Metabolic Diseases*
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Frederick L. Stone	*Director, National Institute of General Medical Sciences*
Edward F. MacNichol, Jr.	*Director, National Institute of Neurological Diseases and Blindness*
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Paul Kotin, M.D.	*Director, Division of Environmental Health Sciences*
Thomas G. Bowery	*Acting Director, Division of Research Facilities and Resources*
Eugene A. Confrey	*Director, Division of Research Grants*
William B. DeWitt	*Acting Director, Division of Research Services*
Milo D. Leavitt, Jr., M.D.	*Director, Fogarty International Center for Advanced Study in the Health Sciences*

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*Denotes "Miss"

National Institutes of Health

Fiscal year 1968 substantially changed the organization and broadened operational scope for the National Institutes of Health (NIH).

The April 1968 reorganization of the health services of the Department of Health, Education, and Welfare combined the National Institutes of Health, the Bureau of Health Manpower, and the National Library of Medicine into a new and enlarged NIH structure. At the same time, the Division of Regional Medical Programs was transferred from NIH to the Health Services and Mental Health Administration.

A major purpose of the reorganization was to place under unified direction related responsibilities for health research and health education. Previously, by congressional mandate, NIH had supported medical research, construction of health research facilities, and research training, while the Bureau of Health Manpower supported basic professional education.

Passage of the Health Manpower Act of 1968 extended educational assistance and health research facilities programs. The act also provided for construction of new facilities and other assistance that would enable the training of more people in existing facilities and improvement of the quality of the training they receive.

During the year, planning was completed for the John E. Fogarty International Center for Advanced Study in the Health Sciences, which will replace the Office of International Research as the organizational unit responsible for NIH international activities. The Fogarty Center memorializes the late Rhode Island Congressman, who for many years led congressional efforts to expand Federal health research and other health programs. The center will include an international conference and seminar program, a scholars-in-residence program, an international fellowship and exchange program, and a foreign visitor center.

In carrying out its research mission, NIH conducted extensive laboratory and clinical research programs in its own facilities, and continued to support biomedical investigation in medical and dental schools, universities, and other research centers throughout the country.

Research Accomplishments

In the intramural program, NIH investigators—

- Produced a pushbutton painkiller, which allows a patient to "turn off" the excruciating pain of angina pectoris. The painkiller's transmitter activates an electronic system under the patient's skin, which "kills" the pain by producing a series of reflexes that reduce the heart rate, relax the heart, and lower blood pressure in the arteries.
- Discovered, while studying the rare "Tangier Disease," some of the secrets of how the blood carries fats. Since abnormal fat transport is one of the causes of arteriosclerosis, which causes more than twice as many deaths as any other disease, this discovery is a vital one.
- Developed an experimental heart massaging device which may prove to be a valuable hospital emergency room tool. When fitted around a failing heart, the device helps restore normal heart beat.
- Isolated a new thyroid hormone that, by its ability to regulate calcium in the body, promises to be important in treating several bone-destroying diseases.
- Developed an artificial lung that may help doctors save the lives of premature babies suffering from respiratory distress syndrome, or those with severe heart defects.
- Helped refine a rubella vaccine which may produce immunity without spreading infection.

NIH also supported many outstanding research projects outside the Institutes, including:

- *The University of Utah* successfully tested two prototypes of an inexpensive artificial kidney machine (costing about $600) that could, by replacing machines costing up to $10,000, make treatment available to thousands who cannot now afford repeated trips to the hospital. Research on mass production continues.
- *Childrens Hospital in Philadelphia* implicated a herpes-type virus as the probable cause of mononucleosis, a contagious disease of the blood that afflicts 10,000 Americans annually. This may lead to development of a vaccine.
- *Cornell University* produced the first completely synthetic antibiotic, terramycin, through a method that may lead to the manufacture of other drugs tailored to combat specific infections. The molecular engineering process used can now be applied in production of other compounds.
- *Johns Hopkins University* produced a small, wristwatch-like sensor that can measure, through the intact skin, the amount of

carbon dioxide in a patient's bloodstream. The device can detect abnormal breathing danger signals, and may reduce mortality from acute respiratory syndrome and emphysema.

Bureau of Health Manpower

Under the stimulus of the growing shortages in all categories of health manpower, and with the increased interest and support of the President and the Congress, the Bureau of Health Manpower continued in 1968 to devote its full energies and resources toward—

- Increasing the capacity of health-related educational institutions and improving the quality of their programs.
- Upgrading the knowledge and ability of health practitioners.
- Encouraging better utilization of scarce skills.
- Interesting young people in health careers.
- Enlisting greater cooperation among public, voluntary, professional, educational, and industrial agencies and groups in concerted attacks on the many facets of health manpower.

Expenditures in fiscal year 1968 totaled $203 million in construction grants and $150.9 million for all other programs, compared with 1967 expenditures of $160 million for construction and $133.7 for other purposes.

DIVISION OF ALLIED HEALTH MANPOWER

The Division of Allied Health Manpower operates programs supporting the education of manpower for allied health and public health occupations and specialties.

In 1968, a total of $9.75 million in basic improvement grants was distributed to 230 junior colleges, colleges, and universities, to improve and strengthen their allied health educational programs.

Advanced Training

Grants for advanced traineeships totaling about $1.2 million were awarded to 49 colleges and universities for 257 trainees preparing to teach or to serve in administrative, supervisory, or specialist capacities.

New Occupations

Sixteen grants totaling $799,507 were awarded for the development, demonstration, and evaluation of curriculums for new types of health technologists such as physical therapy assistant, orthopedic assistant, and extracorporeal circulation specialist.

Construction

One construction grant for approximately $1.8 million was awarded which will more than double the grantee institution's student enrollment capacity in seven allied health programs.

Public Health Training

Graduate or specialized training in public health was provided for about 1,400 trainees through long-term, residency, and apprenticeship programs. In addition, 10,000 health workers received short-term training and continuing education in public health.

Special project awards totaling about $4.5 million were made for 124 graduate programs in schools of public health, nursing, engineering, medicine, and dentistry. The projects were designed to strengthen or expand graduate or specialized public health training in such areas as environmental health, preventive medicine and dentistry, public health administration, accident prevention, and medical care economics and administration. In addition, awards totaling $4 million went to the 15 schools of public health for basic educational programs support.

Special Programs

During 1968 the Division of Allied Health Manpower initiated two special programs. One is a nationwide recruitment and counseling program designed to attract people to the health occupations. The other is a study to determine the role and function of a person who might be prepared to assist the anesthesiologist.

THE DIVISION OF DENTAL HEALTH

The Division of Dental Health concentrates on manpower and education, community programs, and dental technology.

Under the Health Professions Educational Assistance Act, grants were awarded for the expansion of two existing dental schools and for the construction of three new schools, for a total of 201 additional class places.

Increasing Productivity

Under the Division's experimental program in dentist productivity, qualified dental assistants, as members of experimental teams, are performing clinical procedures normally performed by dentists. The teams, composed of one dentist, four full-time chairside assistants, and one supply-sterilization assistant, work together in a four-chair operatory.

Forty-eight dental schools—8,810 students—participated in the Division's dental auxiliary utilization (DAU) program, teaching dental students the effective use of trained chairside dental assistants. This instruction is now standard in all fully operational American dental schools.

Awards of grants for this program total $3 million for the past year, the largest in the history of the program. Since its initiation

6 years ago, the program has provided training to almost 22,000 graduates.

New Information and Methods

A National Dental Data Compilation System, developed jointly with the American Association of Dental Examiners, published data on personal and professional characteristics of the dentists licensed in 18 States. A second-cycle survey is now underway with questionnaires to dentists in 21 States.

Data on licensed dental hygienists in the participating States were collected and a format has been devised to report these data to the States.

Studies of the advance elements of undergraduate dental education were undertaken in five areas—recruitment and selection of dental students, development of dental teachers, educational administration, design of institutional facilities, and methods of instruction.

Through grants, contracts, course development, and field activities in continuing dental education, the Division has contributed considerably to nationwide activity. Approximately 50 percent of the States are engaged in continuing education systems development.

Two new and three continuing grants were awarded in fiscal year 1968. Contracts included surveys throughout the six New England States, the Southern, Midwestern, and Western States to identify dentists' needs and preferences in continuing education.

Four demonstration courses utilizing programed, group-teaching machines and other communication media were presented in 13 States to 2,285 participants in 1968. Since the start of the program in 1965, programed instruction courses have been demonstrated in 27 States to over 10,000 participants.

Public Health

The Division has continued to provide consultation and technical assistance to the dental components of Project Head Start, neighborhood health centers, Job Corps, and VISTA. Site visits were provided to all programs needing direct consultation or technical assistance.

A self-contained mobile dental unit, developed by Division staff, now is being used in OEO projects in Tennessee.

Disease Prevention

Coordinated statewide approaches to fluoridation have resulted in more rapid extension of the benefits of fluoridation of community water supplies. Delaware and Michigan passed laws making fluoridation available statewide. Massachusetts repealed a law which had required a referendum prior to the institution of fluoridation. Detroit, with a water system serving over 3 million people, joined the list of major cities now having fluoridated water supplies. Approximately 82 million persons in the Nation, slightly over half using public water supplies, now have access to fluoridated water.

A survey of the current status and trends in prepaid dental care indicated that an estimated 5.2 million persons now have prepayment coverage, compared with 1.2 million in 1963.

Studies to determine the effects of good oral hygiene practices have continued. One project studied the oral hygiene status and habits of more than 2,000 schoolchildren of low-income families in San Francisco.

In Israel and cooperating institutions throughout the United States, the Division's dental technologists are studying new and conventional dental restorative materials in man. The records of more than 1,500 paired restorations have been prepared for review by computer to reveal the clinically significant variances in the materials and techniques tested.

During fiscal year 1968, 445 faculty members or graduate students, from 13 of the Nation's dental schools, and from Federal, State, or local health agencies' staffs, received training designed to improve their research skills. Four programed instruction courses presented by teaching machines provide the initial framework for a series of research seminars and lectures specifically designed to meet training needs.

As of June 30, 1968, 41 active research grant projects for a total of $1.26 million were supported through research grants. In fiscal year 1968, 18 new grants were approved in the total amount of $769,246.

International Dentistry

At the Division's dental health center in San Francisco, 73 dentists from 29 countries received training designed to provide ideas, skills and materials which they can take back to their own countries.

DIVISION OF HEALTH MANPOWER EDUCATIONAL SERVICES

Improvement Grants

Special health professions educational improvement grants totaling more than $10,131,000 were awarded for the first time in 1968 to 48 schools of medicine, dentistry, optometry, osteopathy, and podiatry for the best proposals for overcoming academic weakness created by financial need.

Basic improvement grants, totaling nearly $32.2 million were awarded to 270 health profession schools to improve the quality of the educational experience and to aid in supporting increases in enrollment.

Table 1.—***Health professions educational improvement grants in fiscal year 1968***

Type of school	Basic grants		Special grants	
	Number	Amount	Number	Amount
Medicine	99	$20,242,500	23	$5,476,610
Dentistry	51	8,859,500	11	2,689,059
Optometry	10	1,360,500	7	637,610
Osteopathy	5	1,063,000	2	410,299
Podiatry	5	635,000	5	918,127
Total	170	32,160,500	48	10,131,705

Table 2.—***Budgeted amounts by categories of expenditures in fiscal year 1968***

Category	Basic grants		Special grants	
	Percent	Amount	Percent	Amount
Teaching staff	64.1	$20,601,415	51.9	$5,259,041
Other staff	12.3	3,957,719	10.8	1,090,719
Equipment	12.3	3,964,189	23.6	2,391,732
Alteration and renovation	5.7	1,825,145	8.6	870,177
All other expenses	5.6	1,812,032	5.1	520,036
Total	100.0	32,160,500	100.0	10,131,705

Student Assistance

Assistance to students continued to increase in 1968 in schools of medicine, dentistry, optometry, osteopathy, podiatry, and pharmacy:

- Second-year students became eligible for scholarships for the first time in 1968, resulting in an increase of 4,164 recipients.
- Nursing student borrowers increased by 7,314, or 6 percent.
- Health professions student borrowers increased some 3,356 or 5 percent.
- The Health Professions Education Fund and Nurse Training Funds provided more direct private support of student loans—a total of $18,122,000 loaned to 534 schools.

Foreign Students

Program and guidance services were provided to 573 new foreign students and 235 carryover foreign students by the foreign students education program. Direct student loans aided 51 Cuban refugees pursuing health professions studies.

Table 3.—***Student assistance program fiscal year 1968***

	Nursing student loans	Health professions student loans	Health professions scholarships
Number of participating programs or schools	690	217	238
Total amount allocated	$16,389,885	$26,659,476	$7,198,000
Total enrollment	101,262	64,460	38,872
Student recipients	24,532	25,383	7,964

DIVISION OF NURSING

The Division of Nursing supported a number of new programs to increase the supply of nursing manpower, improve the quality of nursing services, and communicate and apply new nursing knowledge.

Educational Opportunity Grants

An amendment to the Nurse Training Act authorized nursing educational opportunity grants to enable qualified students of exceptional financial need to pursue nursing education. Through 238 participating schools of nursing, an estimated 7,700 students not otherwise able to attend nursing school received scholarships averaging $535.

An organization operating under the aegis of Boston University, ODWIN (open the doors wider in nursing), is endeavoring through a contract under this program to interest a larger number of Massachusetts nursing schools in attracting and admitting academically and financially disadvantaged students.

Also by contract with the Division of Nursing, the American Nurses' Association (ANA) is working through group leaders in District of Columbia community action agencies to identify eighth-, ninth-, and 10th-grade disadvantaged boys and girls with potential for nursing.

Construction Grants

Under the Nurse Training Act, construction grants were made for the first time to nursing education institutions in Colorado, Iowa, Michigan, Tennessee, Virginia, Washington, and Guam. Besides helping to replace, renovate, expand, and equip nursing education facilities the 23 construction grants awarded this year made it possible to establish eight new nursing programs in community colleges.

Project Grants

Project grants for the improvement of nursing training were awarded to institutions in three States previously not participating—Hawaii, Oklahoma. and Oregon.

Of the 35 new project grants awarded, they are supporting such educational innovations as joint classes to prepare nursing students and students in other health professions for working in teams, and reorganization of a nursing curriculum to help practical nurses achieve professional status.

Program Review

Achievements in these and other programs of aid to students and schools of nursing, as authorized by the Nurse Training Act and administered by the Division of Nursing, were summarized in "Nurse Training Act of 1964—Program Review Report," in December 1967.

Graduate Training and Research

A training program separate from those authorized by the Nurse Training Act—the nurse scientist graduate training grants program—this year was broadened to include support for research training in the communication of scientific knowledge. Previously, awards had been made to train nurses for research in the basic sciences but not in the science of communication. The first nurse scientist graduate training grant was awarded in June 1968 to the University of Kansas, which is strengthening its graduate department of communication and human relations and granting stipends to nurses undertaking doctoral programs.

Public Health Nursing

In cooperation with the District of Columbia Health Department, the Division of Nursing undertook a 2-year controlled study to improve public health nursing preparation and practice in the care of infants.

The study population will consist of 300 first live-born infants discharged to their mothers from the District of Columbia General Hospital and randomly assigned to either a control or experimental group for care by D.C. Health Department nurses over a 1-year period.

Nursing Manpower

The Division of Nursing supported studies of nursing manpower trends, sources, and supply. In one manpower undertaking, the Division contracted with the American Hospital Association (AHA) for a questionnaire survey of its 7,000 member hospitals to determine the number of nurses they employ both full- and part-time, by level of position. The new survey will update nursing information from a 1966 Public Health Service-American Hospital Association investigation to obtain staffing data concerning 34 professional and technical positions. It will also serve to point up nurse staffing changes which have occurred in AHA member hospitals since the advent of Medicare.

Planning

In fiscal year 1968, the Division of Nursing provided technical consultation to the first regional planning effort for achieving nursing services and educational opportunities based on regional needs rather than on State requirements. The Division is providing guidance and technical assistance to the upper midwest nursing study, which is seeking to improve nursing services in Minnesota, Montana, North and South Dakota, and upper Michigan and Wisconsin.

Table 4.—*Fiscal summary*

	Thousands
Support for schools of nursing (Nurse Training Act):	
Projects for improvement in nurse training	$4,000
Payments to diploma schools of nursing	3,000
Nursing school construction grants	19,382
Support for students of nursing (Nurse Training Act):	
Professional nurse traineeships	9,864
Nursing student loan program	16,390
Nursing educational opportunity grants	4,120
Extramural research and research training grants:	
Extramural research grants	2,593
Special nurse fellowships	520
Nurse scientist graduate training grants	580
Direct operations	2,454
Total	62,903

THE DIVISION OF PHYSICIAN MANPOWER

The nation's undersupply of physicians continues to be a problem amplified by the Nation's population growth and the increasing demands for medical care, including care for the aged and the deprived. In 1968, active physicians in the United States totaled 311,000 but this number included those engaged in medical research, education, and administration, as well as those performing health services. Estimates indicate that 50,000 additional physicians are needed to provide adequate health care to the people of the Nation.

The Division of Physician Manpower supports a variety of programs to increase the supply and to improve the education, utilization, and effectiveness of practicing physicians.

Medical School Construction

To increase the number of students entering medical school, the Division awards grants for the construction of new schools and the expansion and renovation of existing schools. First-year places in medical schools (and other health professions schools) resulting from funds awarded under the Health Professions Educational Assistance Act are shown in the table below:

Table 5.—*New first-year student places anticipated from funds awarded under Health Professions Educational Assistance Act*

	Total	Fiscal year				
		1965	1966	1967	1968	1969
Total	3,640	1,038	749	937	702	214
Medicine and osteopathy	1,844	540	405	409	351	139
Dentistry	835	271	111	252	201	---
Public health	357	191	35	126	5	---
Optometry	157	36	41	0	80	---
Pharmacy	367	---	157	150	60	---
Veterinary medicine	80	---	---	---	5	75

Note.—Total of all awards—$433 million. Grants awarded since Jan. 1, 1968—$96 million as of Oct. 16, 1968.

Medical Education

In its efforts to encourage new approaches to the teaching of medical students and physicians, the Division sponsored a conference on the "Use of Computers in Medical Education" and the "Fourth Rochester Conference on Self-Instruction in Medical Education." A project for the retraining of inactive physicians was extended at Pacific Medical Center, California.

To upgrade the training of medical students in community health care, the Division is supporting a study at Marquette School of Medicine, Wisconsin, to develop guidelines for more effective teaching of courses in community medicine.

Continuing Education

In support of continuing education, the Division has continued a variety of projects, including one at St. Luke's Hospital in New York City, where the resources of this major medical center are providing continuing education for many of the hundreds of local physicians who have no hospital affiliation.

A contract with the Postgraduate Medical Institute, Boston, Mass., is evaluating the effectiveness of a consultation service in helping New England community hospitals establish and maintain educational programs for their physicians.

Other continuing education projects are being supported at the University of Wisconsin, Yale University, the University of Washington, Toledo-Lucas County (Ohio), and the University of California.

Supply and Utilization

During the year, the Division launched a study, "How Medical Students Finance Their Education," a survey of the 1967–68 class of all medical and osteopathic schools in the United States. The Division also has joined with the Division of Allied Health Manpower in funding a contract through Emory Medical School in Atlanta, Ga., to study the feasibility of establishing a new health occupation—anesthesiologist assistant.

To increase substantially the productivity of physicians, the Division is studying the development of a new health worker—the physician assistant, with particular reference to the pediatric assistant. At the outset, the role of such an assistant will be analyzed and defined, and an educational program will be developed.

National Library of Medicine

By contributing biomedical information support to institutions, scientists, practitioners, and students, the National Library of Medicine has continued to meet the challenge of explosive growth of scientific literature; tremendous expansion of health research; increasing urgency to apply new knowledge to health improvement; growing specialization of health science, education, and practice; and the introduction of sophisticated automated equipment.

MEDLARS

The National Library of Medicine pioneered establishment of the Medical Literature Analysis and Retrieval System (MEDLARS), which during the fiscal year reached a high of more than 850,000 bibliographic citations stored in a high-speed computer memory bank. In connection with this system, the Library supported six university-based decentralized MEDLARS search centers.

Of special significance was the establishment of a second generation MEDLARS. On June 11, 1968, a contract was signed for the design, development, and program support for a new, more powerful and sophisticated system. MEDLARS II will support library-based information services in the network, provide requirements for processing toxicological information, and improve effectiveness of the Library's internal operations.

REGIONAL MEDICAL LIBRARIES

As part of the grants program authorized by the Medical Library Assistance Act of 1965, grants are available for development of a national system of regional medical libraries. In October 1967, the first such library began operating at the Francis A. Countway Library of Medicine (of Harvard University and the Boston Medical Society). Known as the New England Regional Medical Library, it serves Massachusetts, Maine, Vermont, New Hampshire, Rhode Island, and Connecticut.

In June 1968, the College of Physicians of Philadelphia Library received an award to establish and operate the Mid-Eastern Regional Medical Library, which serves Pennsylvania, Delaware, and Southern New Jersey. The University Health Sciences Library of the University of Washington established the Pacific Northwest Regional Medical Library, which serves Alaska, Idaho, Montana, Oregon, and Washington. The John Crerar Library, Chicago, Ill., designated the Mid-West Regional Medical Library, serves Illinois, Indiana, Iowa, Minnesota, and Wisconsin. The National Library of Medicine serves as the Mid-Atlantic Regional Medical Library, covering Maryland, Virginia, West Virginia, and the District of Columbia.

COMMUNICATIONS SYSTEMS DEVELOPMENT

On April 1, 1968, the National Library of Medicine became part of the reconstituted National Institutes of Health but has continued serving as the Department's center for health communication and related scientific information systems development.

Pursuant to the recommendations of the House Appropriations Committee Report, 1967, and the Rogers Special Subcommittee on Investigation of HEW (89th Cong. 2d Sess., H. Rept. 2266), the Library has established and successfully staffed a program of developmental and engineering work relating to a biomedical communication network. This staff has prepared a preliminary design for such a network, which encompasses medical libraries, specialized information centers, audiovisual communications and related components.

LISTER HILL NATIONAL CENTER FOR BIOMEDICAL COMMUNICATIONS

To house the organizational, managerial, and technical elements of the NLM network, a biomedical communication center is being planned and will be located in an annex building, which will be erected southwest of the Library.

NATIONAL MEDICAL AUDIOVISUAL CENTER

As recommended by the Rogers Special Subcommittee, the National Medical Audiovisual Center in Atlanta, Ga., was transferred administratively to the National Library of Medicine on July 1, 1967.

LIBRARY REORGANIZATION

Assignment to the Library of responsibility for toxicological information and audiovisual production and dissemination, and the establishment of a research and development program in biomedical communication, made reorganization of the Library essential to the successful management of NLM programs.

The new organization, effective January 9, 1968, identified five major programs in biomedical communications within the Library's mission: library operations; specialized information services; audiovisual programs; research and development; and extramural programs. In addition, an Office of Computer and Engineering Services was established.

National Cancer Institute

The avenues of total attack against cancer by the National Cancer Institute and the scientific organizations whose work it supports may be broadly grouped under two classifications: *Cause and Prevention* and *Diagnosis and Treatment.* Progress toward utlimate success in these areas may be measured by several criteria: increased knowledge of the fundamental nature of malignant disease; identification and control of factors involved in cause and prevention; improvements in detection, diagnosis, and treatment leading to increased survival for the patient.

Survival is increasing in some forms of the disease. Cancer of the colon and rectum occurs more frequently than any other form of cancer in the United States. A recently completed study showed a striking increase in survival of such patients for 5 years or longer after diagnosis of their disease.

Five-year survival rates for patients with breast cancer have also gone up, slowly but steadily, and there was some indication of an increase in the number of patients diagnosed when tumors were still confined to the breast.

CAUSE AND PREVENTION

Smoking and Lung Cancer

Cancer of the lung, a largely preventable disease caused mainly by cigarette smoking, continues to increase at an alarming rate. It will claim about 55,000 lives in the United States in 1968 and continue to rank as the leading cause of cancer death in men. Although significant improvement was observed in survival of patients with localized disease, only one in five cancers of the lung was discovered in this early stage.

Leadership in planning and organizing research approaches to the lung cancer problem has been taken by the Lung Cancer Task Force established at the direction of President Johnson and chaired by the Director of the National Cancer Institute. This body, composed of scientists and physicians drawn from Government and the academic community, with liaison representation from the tobacco industry and other interests, has identified the major problems relating to lung cancer and considered lines of research attack that might be directed against them from the viewpoints of cause, prevention, diagnosis, and treatment.

The Task Force recognized that the most promising lines of prevention are cessation or at least a marked reduction in smoking, or the introduction of a less hazardous cigarette. Development of a less hazardous cigarette has been given high planning priority.

The Search for Other Environmental Causes of Cancer

Studies of population groups have provided clues to the causes of various kinds of cancer. A report on stomach cancer in Iceland and another on skin cancer in Taiwan highlighted the importance of environmental factors in cancer induction. In the Icelandic study, a relationship was reported between stomach cancer and dietary differences among various occupational groups. More specifically, the results appear to support evidence of a relationship between stomach cancer and consumption of home-smoked and singed foods. In Taiwan, a clear dose-response relationship was established between the frequency of skin cancer and the arsenic content of the well water used by villagers in different localities.

First reports have become available of some of the results of long-term studies of the cancer experience of Japanese migrants to the United States and their children born in this country. It was found that both groups continued to experience the high stomach cancer and low breast cancer risks characteristic of homeland Japanese, but that their risk of colon cancer changed from the low Japanese to the high U.S. rate.

Initial results of a search for clues to cancer causes through studies of persons with multiple cancers were reported. Data obtained from two large New York cancer centers showed that patients with leukemia, lymphoma, or myeloma were more likely than persons in the general population to develop skin cancer, but that their risk of a second more serious malignancy was not increased.

A review of deaths from childhood neuroblastoma occurring from 1950 through 1964 shed interesting light on the possible causes of this disease. Epidemiologists found an apparent excess number of deaths in certain geographic areas at certain times and noted that neuroblastoma was most often diagnosed in the first year of life. These observations suggest an environmental factor affecting the child before birth.

Viruses as a Possible Causative Factor

Virus studies continued to dominate the field of research on cancer causation. Many investigators were seeking to confirm the exciting results of work by Philadelphia scientists who reported evidence that the herpes-type virus (HTV) previously associated with Burkitt's lymphoma, a cancer of the lymph glands occurring primarily in African children, is closely associated with and perhaps may actually cause infectious mononucleosis.

The HTV has been detected with remarkable frequency in cell lines derived from Burkitt's lymphoma, leukemic tissues, healthy donors, and patients with a variety of diseases; and blood serum surveys have shown that infections by the virus, or a close relative, are frequent and worldwide. However, except for the fact that all Burkitt's tumor patients studied have high levels of antibodies to HTV antigens, no suggestive relationship of the virus to a known disease has been previously recorded.

As the virus-cancer research pace has quickened, it has become quite clear that certain dangers are inherent in this work. Under the leadership of the National Cancer Institute, an educational and developmental program is in progress aimed at protecting personnel and experiments from inadvertent exposure to suspect or known cancer viruses. A laboratory on wheels, the Biohazard Containment Mobile Laboratory, was designed and built under contract as a prototype facility for the Institute. It is presently being used by Institute virologists and will be made available to other research institutions cooperating in cancer virus programs.

A new laboratory building, the Emergency Isolation Facility, incorporating the latest biohazards protective procedures, is under construction on the grounds of the National Institutes of Health, and will be completed early in 1969. It not only will house virus-cancer experiments, but will also enable sanitary engineers and others to test new safety techniques and devices. All virus-cancer studies at the National Institutes of Health have been integrated into the National Cancer Institute program.

DIAGNOSIS AND TREATMENT

Detection of Breast Cancer

Continuous efforts are being made to obtain better results in detecting breast cancer. The techniques under development employ X-rays, heat-sensing devices, and ultrasound. The Institute continued to support an extensive screening and evaluation program for an X-ray method, known as mammography, under a contract arrangement with the Health Insurance Plan of Greater New York. On the basis of comparison between the number of breast cancers detected in the screened group and those in a control group, the investigators have been able to estimate that the program detects breast cancer on an average of 21 months earlier than is possible by clinical examination. The question, however, of whether this method of detection will bring about an improvement in the survival rate of patients remains to be determined.

Treatment Research

In recent years chemotherapy, or treatment with drugs, has been successful in effecting some control over certain forms of cancer known as the fast-growing tumors. These include leukemia, Hodgkin's disease, Burkitt's lymphoma, choriocarcinoma (a cancer of the placenta), testicular tumors, and certain tumors of childhood. As a result of this experience, investigators are beginning to understand the characteristics of cell populations making up tumors, and have begun to adapt the principles learned in these studies to the slowly growing ones. These latter tumors include lung, breast, prostate, and colon and rectum cancers, among others.

Drug Treatment of Leukemia

Studies initiated only a few years ago substantiate the remarkable pace of advancements in cancer chemotherapy. In 1968, at major treatment centers, it was possible to restore 90 percent of patients with acute lymphocytic leukemia—the most common form in children—to complete, though temporary, good health; and most of these patients can be expected to live at least 3 years. As recently as 4 years ago the complete remission rate was 50 percent and the median length of survival only 12 to 19 months.

Another encouraging development is the increasing number of persons surviving more than 5 years after diagnosis of leukemia. The Acute Leukemia Task Force, a group of medical experts assembled by the National Cancer Institute to aid in developing a coordinated research effort in this field, has compiled a worldwide registry of more than 150 long-term survivors. From this data, task force members have concluded that discontinuance of leukemia therapy appears justifiable and perhaps advisable 7 years from diagnosis, if a patient has had no evidence of disease for at least 4 years. This strongly suggests the possibility that, in some cases, leukemia can be considered cured.

Besides the drugs themselves, the technique of administering them in combinations intermittently is given major credit for recent successes in treatment. Four agents most often used have been prednisone, vincristine, mercaptopurine, and methotrexate, but others are also effective and new ones may provide even better treatment combinations in the future. For example, cytosine arabinoside has been found increasingly useful in treating acute lymphocytic leukemia which has become resistant to other drugs, and effective against undifferentiated childhood leukemia and the acute myelocytic form of the disease.

Another agent receiving consideration in clinical trial is L-asparaginase. Clinical trials of L-asparaginase are being conducted in patients with acute leukemia and lymphosarcoma.

Drug Treatment of Other Cancers

Encouraged by successes in treating leukemia with combinations of drugs, physicians have been applying this therapeutic technique to other cancers. Early, or localized, Hodgkin's disease yields to intensive irradiation, but for far-advanced disease, a regimen of four-drug treatment has been found most effective. Thus, adequate radiation therapy and adequate drug therapy provide opportunities for dramatically increasing the cure rate for Hodgkin's disease.

Concurrent use of two anticancer agents, dactinomycin and vincristine sulfate, has produced regressions of solid tumors of childhood without serious side effects, always a problem in cancer chemotherapy.

Investigators administered the two drugs to 18 children, ranging from 8 months to 16 years of age, with nine types of inoperable malignant tumors. All patients improved, and in some of the children response to chemotherapy was such that subsequently the tumors could be removed by surgery or destroyed by radiation therapy.

A drug, melphalan, has been found to produce good response and prolong survival in a high percentage of patients with multiple myeloma, cancer of the plasma cells, or bone marrow. In addition, National Cancer Institute and other investigators have reported that the calcium loss characteristic of this form of cancer can be partially restored by fluoride treatment. Fluoride treatment has also been suggested for metastases (secondary growths of a primary tumor) to the bones of patients with such common tumors as those in the breast and prostate.

The well-recognized dangers of drug treatment have been highlighted in a report by a group of Veterans' Administration investigators participating in the National Cancer Institute's cooperative chemotherapy program. These physicians found out that, although estrogen therapy results in a slight reduction in deaths from cancer of the prostate, it substantially increases the risk of death from cardiovascular disease. In many cases, this risk is justified by the severity of malignant disease; in others, alternative forms of treatment may be indicated.

Although the accomplishments in cancer research have been important and encouraging, the disease problem remains a formidable one. Over the last 30 years the survival ratio of cancer patients has been improved from fewer than one-in-five to one-in-three, and under optimum conditions of early detection and effective treatment could be increased to one-in-two. Yet, despite the steady improvement in cure rate, the death rate is increasing about 1 percent a year, and from this standpoint it may be said that we are losing ground.

National Heart Institute

The special province of the National Heart Institute is the cardiovascular system and its diseases. Its primary mission is to conduct and support research to increase knowledge of the structure and functions of this system and to search for means of preventing, alleviating, and curing the diseases that afflict it. It is a complex system, vulnerable at many points, and prey to a large family of diseases. In many instances, the causes of these diseases are not known. Some may be inherited. Others may arise from adverse factors affecting the fetus at critical stages of development. Still others may evolve from subtle abnormalities in the complex processes of metabolism. In addition, many factors—within the person himself, his surroundings, or his mode of life—may affect susceptibility to these diseases, accelerate their development, or trigger their often devastating complications.

The complexities of the cardiovascular disease problem dictate a research program of considerable scope and diversity. The foundation of the Institute's research effort is its research grants program. During fiscal year 1968 NHI spent $95 million in support of 2,024 cardiovascular research projects at universities, hospitals, and other institutions throughout the country. The results of these projects were promulgated to the scientific and medical communities in more than 4,000 scientific papers and abstracts published during the year by NHI grantees.

Many of these studies yielded basic information on the cardiovascular system and the blood it carries; on the lungs and kidneys that oxygenate the blood and purify it of waste products; and on the nervous system and endocrine glands and their secretions, which influence cardiovascular performance. Some probed deeply into metabolic reactions occurring within individual cells, the enzymes presiding over these reactions, and genetic mechanisms that dictate the form and regulate the production of structural proteins and enzymes. But many other studies provided information, techniques, or instrumentation directly applicable to clinical problems: for example, clinical trials evaluating promising new drugs; safer, more sensitive diagnostic tests for detecting and evaluating inborn or acquired cardiovascular disorders; improved surgical methods, life support techniques, or artificial valves for the management of congenital or rheumatic heart disease; improved monitoring procedures for heart-attack patients and for averting or coping with potentially lethal complications.

ARTIFICIAL HEART–MYOCARDIAL INFARCTION PROGRAM

The NHI artificial heart-myocardial infarction program is combining bioengineering and biomedical approaches to: the development and evaluation of devices and techniques to assist a failing circulation; and reduction of death and disability from acute heart attacks, which are responsible for well over half of the 560,000 U.S. deaths occurring each year from arteriosclerotic heart disease.

One long-term goal is discovery of a completely implantable, permanent artificial heart replacement, but the program is currently concentrating on the development and refinement of a family of devices that provide pumping assistance to patients with acute heart failure. Such devices may save many otherwise doomed heart-attack patients by giving their hearts a temporary respite to mend damage and regain strength before resuming their full circulatory obligations.

During fiscal year 1968 the Artificial Heart Branch awarded 51 new contracts and extended 48 others for studies basic to the development and evaluation of circulatory-assist devices. These awards, totaling $7 million, supported research in 13 key areas of physiology and bioengineering.

The Myocardial Infarction Branch awarded four contracts totaling $2 million for the establishment of Myocardial Infarction Research Units (MIRU's) at the University of California, San Diego; Cedars-Sinai Medical Center, Los Angeles; the University of Chicago; and the University of Rochester. Support was continued for MIRUs previously established at the University of Alabama, Cornell, Duke, Johns Hopkins, and Massachusetts General Hospital.

Each MIRU is a clinical unit within the patient-care area of the hospital specially equipped and staffed for the most comprehensive care and detailed study of heart-attack patients during the acute phase of their illness.

CORONARY DRUG PROJECT

The NHI coronary drug project is directed against still another facet of the heart-attack problem. It hopes to establish that long-term reduction of blood lipids with drugs will confer some degree of protection against recurrent heart attacks and other complications of preexisting coronary heart disease, and reduce 5-year mortality rates by 25 percent or more.

As of June 30, 1968, nearly 5,000 patients had been recruited toward the final goal of 8,500 for the project. Recruitment will be terminated in June 1969, and the study itself should be completed in 1974.

NATIONAL BLOOD RESOURCE PROGRAM

The NHI national blood resource program was established in 1966 to survey our Nation's blood resources and their utilization in terms of present and foreseeable needs; and meet a steadily accelerating demand for blood products without unduly taxing these resources through improvements in technology relating to the production, storage, and distribution of these products.

During fiscal year 1968 the program awarded or extended 21 contracts totaling $1,612,290 for research in four key areas: The development of an integrated system for the mass production of blood fractions; studies of the chemical preservative adenine as a means of extending the storage life of whole blood; studies to determine the feasibility of a computer-based regional or national inventory system for blood products and blood donors; and clinical studies to assess the effectiveness of the clot-dissolving agent urokinase against clots obstructing blood vessels in the lungs (pulmonary embolism).

An important result of this work could be an AHF concentrate that could be prepared in sufficiently large quantities at sufficiently low cost to permit its use as a routine, rather than an emergency, procedure for preventing or controlling hemorrhage in hemophiliacs.

Other contracts are supporting feasibility studies of a computerized inventory system for blood products and blood donors that might be applied on a regional or national basis. If workable, such a system might make possible a more equitable distribution of the blood supply; prevent or meet local shortages through redistribution of local surpluses and reduce losses due to outdating in storage; provide means of summoning potential donors during periods of need; and provide means of locating rare blood donors in a region.

INTRAMURAL RESEARCH

A vital segment of the Heart Institute's overall research program is the basic and clinical research conducted at Bethesda, Md., and elsewhere by members of the NHI scientific staff. Among the results reported during fiscal 1968 were:

- Development of a miniaturized oxygenator that shows promise in the treatment of hyaline membrane disease in infants and in the management of other acute respiratory crises.
- Continued progress in the detection, classification, and treatment, through special diets and lipid-lowering drugs, of lipoprotein abnormalities often associated with premature development of atherosclerosis and coronary heart disease.
- Elucidation of the chemical structure of thyrocalcitonin, a hormone that shows promise in the treatment of various disorders of bone metabolism.
- Successful clinical use of an implanted carotid sinus nerve stimulator to provide almost instantaneous relief of angina pain.
- Continued progress in research on the nature and function of the genetic code that directs and regulates the production of the enzymes and structural proteins of the cell.

TRAINING SUPPORT

In addition to its research program, the Heart Institute also supports a broad program of training grants and fellowships aimed at improving the scope and quality of cardiovascular teaching in our Nation's medical institutions, expanding the available pool of highly trained research manpower in the cardiovascular field, and providing clinical training in the latest methods of cardiovascular investigation, diagnosis, and treatment. During fiscal year 1968 NHI provided $24 million in support of these training activities.

National Institute of Allergy and Infectious Diseases

TRANSPLANTATION IMMUNOLOGY PROGRAMS

When the first human heart was transplanted in December 1967, interest in this exciting frontier of medicine soared, and the need for knowledge of how and why the recipient body normally rejects such foreign tissue became clear. Much of what is presently known about this rejection phenomenon, or immune response, has been gained through the efforts of scientists participating in transplantation immunology programs of the National Institute of Allergy and Infectious Diseases. During fiscal year 1968 NIAID funds supporting research in this area amounted to more than $5 million. Studies involved laboratory investigations of the rejection phenomenon and developmental research focused on new ways to store organs until needed for transplantation. More efficient ways to collect and distribute information on the total transplant experience also were explored.

Most transplant operations to date have involved the kidney. An analysis of data based on 1,741 kidney transplants reported to a kidney registry supported by NIAID showed kidneys from related living donors have a 1-year survival of 75 percent and a 2-year survival of 67 percent. Kidneys from cadaver (unrelated) donors have a 1-year survival of 45 percent and a 2-year survival of 38 percent.

VACCINE DEVELOPMENT

In the field of vaccine development encouraging news from field trials of a rubella (German measles) vaccine was a highlight of 1968. In an NIAID-supported study, 90 percent of some 6,000 Taiwan schoolchildren given the vaccine were protected in the face of rubella epidemic. If the disease can be more or less wiped out by vaccines, and pregnant women thus shielded from the risk of infection, many birth defects can be prevented.

Work on the development of a vaccine against the principal types of pneumococci was initiated during the year. Ultimate goal of this contract program is a single preparation that will prevent approximately one-third of the estimated 55,000 to 70,000 deaths now caused each year by pneumonia and influenza.

Ongoing research on viruses and vaccines during the year resulted in the development of a new method of preparing vaccines and a new way of administering them. Grantees in Texas found that inactivation of viruses by light resulted in a vaccine which, in animal tests, surpassed the usually formalin-killed virus vaccine in inducing an immune response. In other studies, intramural scientists working with University of Maryland investigators reported that a nasal spray immunization method holds promise in influenza prophylaxis.

CHRONIC DISEASES

At NIAID's Rocky Mountain Laboratory, Hamilton, Mont., scientists continued work on selected chronic diseases of animals that resemble some human disease. A virus which appears to be the cause of progressive pneumonia of sheep was isolated. Work is now in progress to determine whether it, or similar viruses, cause some of the degenerative diseases of man.

ACUTE INFECTIONS

Work on acute infections was wide ranging. For example, a NIAID research career awardee reported serologic evidence that a virus recently associated with a form of cancer known as Burkitt's lymphona was probably the causative agent of infectious mononucleosis; and NIH scientists produced long-term cultures of cells from mononucleosis patients—thus providing an important tool for further studies of this disease.

In another study, NIAID investigators were able to transmit monkey malaria to man by mosquito bite—the mode of transmission occurring in nature. Should it be possible to complete the cycle—to retransmit the disease to the monkey via the mosquito—the implications for malaria control are significant.

ALLERGIES

The problems of hay-fever sufferers and other persons with allergic disorders were studied by a number of NIAID-supported scientists. Clinicians treating patients with medically resistant asthma reported progress through use of prolonged assisted ventilation plus a muscle-relaxant drug. These grantees also identified some of the factors leading to the medically resistant state: infection, fatigue, and overuse of aerosols of epinephrine and similar drugs.

INFORMATION

A number of steps were taken during the last year to alert both the scientific community and the general public to research developments within the Institute's purview. Three major reference catalogs on tissue typing sera, arboviruses, and research reference reagents were compiled and distributed to scientists participating in Institute programs and to other interested investigators. A symposium on public health problems in Arctic populations was cosponsored by the Institute and the University of Alaska. Some 50 participants from several countries discussed threats to health brought on by the expansion of technology into primitive societies of the circumpolar regions. In another symposium, scientists representing many different fields came together to consider the possible causes of emphysema. These experts gave special consideration to the selection of a suitable laboratory animal for studies of this increasingly important lung disease.

The Institute played an active part in the production of "The Miraculous Pool," a film depicting steps in the vaccine development program of NIAID and other activities of the National Institutes of Health. The film was produced by a private foundation at no cost to the Government. The Institute contracted for 100 prints and film distribution, and more than 200 showings by television stations across the country helped report this research progress to the public.

National Institute of Arthritis and Metabolic Diseases

In its research on a broad array of chronic diseases with long-term disabling effects, the National Institute of Arthritis and Metabolic Diseases (NIAMD) seeks primarily to understand their complex mechanisms and bring about more effective, rational treatment and, where possible, prevention. Within the Institute's purview are various forms of arthritis, connective tissue disorders, diabetes, gout, cystic fibrosis and other metabolic disorders, diseases of the gastrointestinal tract, liver, and gallbladder; disorders of nutrition and endocrinology; urologic disorders and diseases of the kidney, artificial kidney development and a related kidney transplant program; diseases of blood, bone, and skin, and orthopedic surgery.

ARTHRITIS

During the year research supported by the Institute strengthened the hypothesis that infectious agents may be involved in causing rheumatoid arthritis. Investigators produced arthritis in both monkeys and rabbits by injecting them with *Bedsonia* organisms isolated from human patients with Reiter's syndrome, a disease closely related to rheumatoid arthritis.

Among numerous drugs under clinical trial are cyclophosphamide, which has produced favorable results in treating certain types of rheumatoid arthritis, and shows promise in treating certain cases of osteoarthritis, a common arthritic disorder associated with degenerative changes in the mechanical structure of joints.

LESCH-NYHAN DISEASE

Institute scientists pinpointed an enzyme defect in Lesch-Nyhan disease, a grave inherited metabolic disorder of childhood, marked by cerebral palsy, self-mutilization, mental retardation, and overproduction of uric acid.

Following this discovery, the researchers developed a urinary screening test with which early detection of Lesch-Nyhan disease now is possible. The procedure also can detect certain cases of gout.

DIABETES

Specific pathological tissue and molecular changes fundamental to diabetes are being examined. Insulin, long thought homogenous, was shown to be present in man in two distinctly different forms. In another study, a substance, "proinsulin," was identified. This is believed to represent the first step in the biochemical formation of insulin.

ARTIFICIAL KIDNEY AND TRANSPLANT PROGRAM

In the past year a diet restricted to small quantities of high-quality proteins but furnishing unlimited carbohydrates and fats was shown to prolong for several months the comfortable life of patients in end-stage kidney failure. The diet can serve as a stopgap measure while the patient with chronic renal disease is considered for dialysis (blood cleansing through the artificial kidney machine) or for kidney transplantation.

Extensive research is now underway on the biochemical and physiological characteristics of the uremic end stage of chronic kidney failure. Meanwhile, a series of new artificial kidneys is under development in the search for more efficient and less expensive dialysis methods.

One very compact "hollow fiber" kidney, simulating the human kidney's network of blood capillaries, has been used successfully during recent months in human patients.

Prognosis for liver transplants, a relatively new procedure, is continuing to improve, with a few young recipients surviving up to a year or more.

NUTRITION

One major effort is aimed at alleviation of malnutrition and nutritional deficiencies (such as iron-deficiency anemia) both in the United States and abroad. The Institute continues to contribute to an understanding of the physiologic and metabolic actions of the various nutrients and their requirements in man. In India and the Philippines the Institute is engaged in developing and evaluating new and inexpensive protein sources for undernourished peoples.

"Facts About Nutrition," published by the Institute this year, became a best seller after radio and television public service broadcasts informed the public of its availability.

National Institute of Child Health and Human Development

By the end of fiscal year 1968 the National Institute of Child Health and Human Development, established in January 1963, had completed its first 5 years.

The legislation authorizing the Institute recognized, in the early 1960's, the urgent need to stimulate, support, and develop research into the nature of human development.

Institute research during fiscal year 1968 concerned the health of infants, children, adults, and aged persons, and the causes and significance of biological and behavioral changes in both normal and abnormal aspects of the human development.

Among the Institute's major efforts were—

- Research in the areas of poor nutrition, and how this affects the childbearing woman and her progeny;
- Research into population problems, including demographic studies and studies to develop safer, more acceptable, and more effective contraceptives;
- Research into the disease conditions of infancy: blood incompatibility caused by the Rh factor, respiratory distress in the newborn, the sudden death of apparently healthy infants in the first few months of life;
- Research extending over the lifespan of individuals and generations, to explore the biological and behavioral consistencies and inconsistencies within the individual and between generations in the same family;
- Research concerned with mental retardation—its causes, prevention, and treatment.
- Research in aspects of human behavior such as how children acquire values and how changes in our culture affect personality structure within the individual.

Not only does the Institute deal with biomedical investigation but also with social issues such as: How we can cope with a rapidly expanding population; how we can reduce infant deaths; how we can prevent mental retardation, which imposes a serious emotional and financial drain on parents; how we can learn more about the aging process, which may eventually alleviate some of the health and social problems faced by the aged.

EXTRAMURAL ACTIVITIES

The Institute now is supporting 1,500 grants totaling $53 million, three-fourths of which represents research grants and one-fourth, research training, a substantial increase from the 1,000 projects totaling $27 million for 1964.

INTRAMURAL ACTIVITIES

The fiscal year 1968 marked the first full year of operation of the intramural research programs. Of primary importance was the completion, occupancy, and dedication of the Gerontology Research Center Building at the Baltimore City Hospital, Baltimore, Md.

In other significant moves, the Children's Diagnostic and Study Branch, the Behavioral Biology Branch, and the Laboratory of Biomedical Sciences, which had previously cooperated in studies of mental retardation at the National Naval Medical Center, were given separate resources and independent bases of operation during the past year.

The Institute was designated the National Institutes of Health focal point for population control and family planning research, and additional funds allocated for contract support resulted in several investigations of the medical effects of oral contraceptives and other aspects of family planning. Contracts were awarded to Kaiser Permanente Medical Care Program, Oakland, Calif.; St. Mary's Hospital, London, England; and the University of California at Los Angeles, Calif. Over 15,000 women will participate in these studies.

Significant Publications

Optimal Health Care for Mothers and Children: A National Priority summarized five meetings with groups of consultants in the fields of obstetrics and gynecology, pediatrics, behavioral sciences, nursing, and social work.

The Institute also published the proceedings of a conference on the *Prevention of Mental Retardation Through the Control of Infectious Diseases*, the first of a series which will cover research and clinical problems relating to the prevention of mental retardation.

RESEARCH RESULTS IN POPULATION DYNAMICS AND REPRODUCTIVE BIOLOGY

Despite a 25-percent decline in the U.S. birth rate since 1957, there still is little evidence that today's average American family will ultimately be much smaller, according to an Institute-supported study at the University of Wisconsin and Princeton University. Instead, the study explained, the 10-year decline in the birth rate is a result of an increase in the average age of wives at childbearing—largely a consequence of a trend towards later marriage—and an increasing tendency to space childbearing over a longer period of time.

MATERNAL AND INFANT HEALTH

In 1967, more than 78,000 infants in the United States died during the first year of life—an infant mortality rate of 22.1 per 1,000 live births, or a drop of six percent compared with 1966. This represents the most significant drop in infant death rates in more than a decade. Diet, drugs, environmental influences, heredity, maternal illnesses, and social factors have been found to have a profound effect on the well-being of the unborn child.

However, one health hazard to many infants, the presence of Rh blood incompatibility, which has caused the deaths of approximately

5,000 infants per year, may be eliminated in the next few years as a result of Institute-supported research. An anti-Rh preparation designed to prevent a mother with Rh-negative blood from becoming sensitized to her infant's Rh-positive blood has been developed, used successfully in a large number of cases, and is now generally available.

RESEARCH RESULTS ON THE DEVELOPING YEARS

An investigator at Harvard University, under contract with the Institute, is studying early cognitive development as related to social class and maternal behavior in children of middle- and lower-class backgrounds. Preliminary analyses of his data suggest that the effects of social class become evident earlier for girls than for boys, and are reflected most clearly in early patterns of vocalizations.

Two Institute grantees at the University of Minnesota, Minneapolis, Minn., have found that culturally deprived children appear to value school and school books highly, at least at the beginning of their school careers, but that their attitudes toward school become increasingly negative with time. They also found that the same phenomenon occurred in a group of middle-class controls. These findings suggest that schools themselves may be a major cause of the negative attitudes of culturally disadvantaged children toward education, and that the schools are failing in one of the most important objectives of education—that of maintaining a positive attitude toward school by the students.

RESEARCH RESULTS ON NUTRITION IN INTELLECTUAL DEVELOPMENT

The science of nutrition has moved beyond traditional concepts of simple deficiencies and minimum requirements. Now attention is being directed toward patterns of nutrient intake which may result in optimum body development and composition, and perhaps also in the achievement of maximum intellectual ability.

One of the most exciting new findings in pediatric nutrition concerns the effects of diet on the development of intellectual capacity. For years, the brain and central nervous system have been considered to be untouched by nutritional variations. Recent studies have greatly modified this concept. In an attempt to explore this concept more fully, the Institute is supporting a contract for a prospective long-term study in rural Central America. Two similar groups of children are being compared, one with an improved diet and the other with the conventional diet of the region. The project focuses on the entire physical and mental development, beginning with nutritional studies of family units and following pregnant women through pregnancy and delivery.

RESEARCH RESULTS IN MENTAL RETARDATION

The Institute has made a heavy investment in the study of the behaviorial and biological aspects of mental retardation. During the past 3 years, 12 institutions have received awards from the National Institutes of Health for the construction of mental retardation research centers, which promise to make a significant contribution in efforts to prevent, diagnose, and manage mental retardation.

Two Institute-supported researchers at the George Peabody College for Teachers in Nashville, Tenn., have found that basic personality factors may be more important than material rewards in determining the level of performance. These researchers found that retardates who achieved satisfaction through the actual performance of a task performed better under the promise of another task than they did under material—money—or no-reward conditions. On the other hand, hildren whose satisfaction came mainly from the ease, safety, comfort, security, and material rewards of the environment performed better under money incentives than under either of the other reward ditions.

RESULTS IN AGING RESEARCH

The new Gerontology Research Center, when fully staffed, will provide space for approximately 400 research workers. It is the largest center for gerontological research in the world and will provide regional, national, and international stimulus to gerontological research.

The new facility will permit expansion of the Center's programs of research related to alterations occurring in the human being during the aging process.

Another area in which the Institute has been active in the past year is retirement. Little is known about retirement and postretirement phases of life, partly because the presence of large numbers of people in this period of life is a recent phenomenon. To help launch a research effort on the phenomenon of retirement, the Institute began a series of conferences, bringing together experts in aging, medicine, social sciences, and administration for an analysis of this critical period and its problems.

National Institute of Dental Research

PREVENTING TOOTH DECAY

Three times a week, 300 preschool children of U.S. Coast Guard families on Governors Island, N.Y., visit the dental clinic to make their own contribution to a tradition of service. Under the supervision of a dental hygienist, they apply to their teeth for 3 minutes a custom-fitted mouthpiece filled with a cherry- or lime-flavored fluoride gel.

Participating in a study by the National Institute of Dental Research, they are testing a new method of topical application of fluoride. If it works, the youngsters will not only benefit themselves but will also help to free future generations of children from the pain of dental caries.

Virtually all children are susceptible to tooth decay. At school age, the average child has three decayed teeth, and by age 15, he has 11 of them. It is hoped that fluoride applications at an early age will provide a foundation for defense that will be maintained longer.

In earlier tests in a community which does not fluoridate its public water supply, this technique reduced tooth decay in school age children by 80 percent. Another study of junior high school students now underway in Charlotte, N.C., is examining whether increased protection may be expected where caries incidence is already low due to water fluoridation. Of particular public health interest is that a single dental hygienist, using this method of application, can supervise several hundred children—many more than is possible with current techniques of topical treatment.

Clinical trials of this technique were begun following successful laboratory studies by scientists at the National Institute of Dental Research. Observing its 20th anniversary this year, the Institute pioneered in research leading to water fluoridation. Now, a continuing area of study is aimed at increasing the benefits of fluoride. The Governors Island and Charlotte studies illustrate the work that is being carried out in this area.

Another approach to the problem of tooth decay focuses on bacteria, since dental caries is due to an interaction between decay-causing bacteria, carbohydrates in the diet, and susceptibility of the teeth. A major accomplishment of the past few years has been the identification of specific microorganisms as a cause of dental caries. Now it is known that these bacteria secrete a sticky material (dextran) which enables them to adhere to the smooth sides of teeth in a film called dental plaque. Held fast in the film, the bacteria bathe the teeth in cavity-producing acid which they produce by fermenting carbohydrates, especially sugar. This new research lead holds promise for one of the most effective approaches in preventive dentistry in recent years.

Preliminary collaborative research with industrial scientists shows that, when a specific enzyme known as dextranase is given to animals in food and water, it almost completely prevents the formation of plaque and the production of smooth-surface caries by the bacteria. Clinical trials are planned.

Still in an experimental stage, a new technique developed by grant-supported investigators seals the pits and fissures in the grinding surfaces of teeth with a plastic mixed with fine silica particles. The adhesive wears off in time but reportedly gives excellent protection against tooth decay for 6 months. Grinding surfaces are the ones most susceptible to caries.

PERIODONTAL DISEASE

Studies of periodontal disease (pyorrhea) continue to shed light on this complex problem. The chief cause of tooth loss after age 35, periodontal disease eventually affects nearly everyone. For the first time, studies of diseased human gingival tissue have shown the presence of the enzyme hyaluronidase. This enzyme is antagonistic to a component of the cementing substance between fibers of the normal gums and leads to a breakdown of these tissues.

Hydrogen sulfide, a waste product of at least five types of microorganisms found in crevices between teeth and gums, has been identified as another suspect in periodontal disease. Institute scientists have detected this gas in gum pockets and are now studying its effects on periodontal tissues.

RESTORATIVE MATERIALS

Until oral disorders can be prevented, most people will require some kind of restorative service. At present, the restoration of decayed teeth requires that the filling be locked in mechanically. This necessitates the removal of sound tooth structure. If an adequate adhesive filling material were available, it would be necessary to remove only the diseased part of the tooth, thereby also reducing discomfort and treatment time. The development of an effective adhesive filling material therefore has high priority in the Institute's research efforts.

One research path has led to the natural cement that holds barnacles to ship hulls, piers, and buoys. To encourage further research into the chemical and physical properties of this cement and its synthetic preparation, the Institute published and distributed a report on scientific progress to date entitled "Barnacle Cement as a Dental Restorative Material."

Research has shown that, in spite of their small organic content, transplanted teeth from a different donor do sensitize a recipient. Thus, rejection is to be expected unless the immune response is suppressed or tissues can, in some way, be matched. These findings emphasize the need to develop synthetic teeth of nonallergic material as replacements for missing teeth. One project of this type, supported by the Institute, involves acrylic plastic teeth. Such teeth have been implanted in the jaws of baboons to replace natural teeth and thus far have remained firm for 7 years.

GROWTH AND DEVELOPMENT

This year, 6,000 new babies will join the ranks of over a quarter of a million persons in the United States born with some form of cleft lip or palate, or both. Several environmental hazards in pregnancy appear to be related to clefting. Seeking more clarification of the metabolic processes involved, the Institute is supporting studies of the effects of drugs in animals that closely resemble man.

Although hereditary aspects of cleft palate are difficult to study in man, they are being explored by Institute geneticists. They find that not only do clefted patients have more birth defects of other kinds than the general population but also their relatives are more likely to have serious abnormalities.

Continuing emphasis is placed on improving diagnostic and rehabilitative techniques, including surgery and speech therapy, to enable cleft victims to achieve near-normal appearance and function. A multipronged research program is also yielding valuable data on the psychological aspects of cleft deformities.

Institute investigators have developed an animal model system to study effects of excess vitamin D in pregnancy. Blood vessel and dental malformations, including malocclusion, have been produced in newborns. Since malocclusion in human patients seems to be increasing in frequency, it may be significant that some pregnant women consume many times the daily dosage of vitamin D recommended by nutritionists. Any possible relationship, however, needs to be further studied.

OTHER DISORDERS

A new finding helps to explain why certain viral diseases, such as fever blisters, persist even though antibodies are built up against them by the body's defenses. It is now known that a virus can combine with its antibody without losing infectivity.

Through other studies, the Institute continues to seek the causes and to improve treatment of oral cancer and of oral ulcers.

National Institute of General Medical Sciences

Traditionally, this Institute supports biomedical sciences that provide data about the nature and structure of man, especially those sciences basic to the research components of the National Institutes of Health.

In addition, the Institute identifies, and applies its research capabilities to, major public health problems.

Unexpected and life-threatening complications encountered in the normal use of drugs, for example, continued to undergo intensive investigation. Research leading to the automation of clinical laboratories to speed and improve the diagnosis and treatment of disease also progressed. New research projects focused sharply upon trauma, the fourth leading cause of death and the foremost cause of disability in the United States.

PHARMACOLOGY/TOXICOLOGY

Using funds provided by the Institute's special program in pharmacology and toxicology, teams of scientists in seven large university research centers have been working to secure comprehensive knowledge of the way drugs are broken down in the human body and how they act upon physiological processes. The teams also have been trying to determine how different drugs interact, one to another and with other chemicals which occur naturally in the body or which may be received from the environment. Information gained from these studies is vital to the safe and effective use of drugs, and to the development of new drugs to combat many kinds of disease.

Receiving particular attention were drugs which cause adverse reactions and the hazardous side effects associated with long term use of drugs. Investigations in this area were expanded by a new project at Baylor University School of Medicine, Houston, Tex., in which scientists are exploring effects in newborn children from drugs administered to their mothers during pregnancy. Drugs under study include those used to control weight, blood pressure, neurological disorders, infectious diseases, and inflammation. Parallel studies are examining the effects of drugs used to combat illnesses and diseases in infants and young children, who react to drugs quite differently than adults because of their immature body processes.

Other scientists have developed a central, computerized system for monitoring and evaluating the results of drugs administered to hundreds of patients in five Boston hospitals. Now being introduced in a number of clinical drug studies supported by the Institute, this system could become a model for adoption by hospitals throughout the country. Over the past year it has been used to spot quickly trends of adverse reactions caused by individual drugs, and by drugs given in combination. It also has led to the discovery of important relationships between drugs and the genetic makeup of patients, including sex and blood type, plus variations in drug effects with patient age. For example, a drug widely used to prevent blood clotting was found to produce serious bleeding far more often in older female patients, and at much lower doses, than in males or young women. Other evidence was obtained that barbiturates behave quite differently in persons with different blood types. Such information makes it possible to identify and protect persons who may be susceptible to harm from particular kinds of drugs.

AUTOMATED CLINICAL LABORATORIES

Biomedical engineering—the application of engineering principles to problems in biology and medicine—centered on activities leading to the automation of clinical laboratories.

Studies of disease and of patient responses to therapy have in recent years become increasingly dependent on clinical laboratory findings. As a result, the clinical laboratory occupies a crucial position in medicine. While progress has been made in partially automating a few analytical techniques, laboratories for the most part are handicapped by time-consuming manual methods and are unable to cope with new demands for services. Hospital admissions have escalated sharply and physicians often request complete lab workups for nearly all patients admitted. Nearly one billion laboratory tests were performed in the past year and the workload is expected to double in the next few years.

The inability of clinical laboratories to keep pace with demand has, in many instances, caused unconscionable delays in getting vital information to physicians, and pressure for more and more tests has gravely imperiled laboratory accuracy. Health authorities are agreed that the problem can only be solved by totally automating clinical laboratory operations.

By supporting a carefully programed mixture of basic and applied research activities, the Institute is seeking to develop a single online analytical system capable of performing rapidly and accurately a broad spectrum of multiple analyses on minute samples of tissues, blood and other body fluids.

One such unit in advanced development combines collection and calculation of body chemistry data from laboratory instruments, transfers the results to electronic reporting media, and blends bookkeeping and laboratory test results into a system which promises to reduce substantially hospital staff time.

In the area of badly-needed new instruments, advances have been made in development of laser microprobe technology for histo- and cytochemical analysis, including trace metal analysis. This technique permits ultramicro concentrations of zinc, magnesium, and other trace elements to be measured within a single cell. Beginning with vaporization of a tissue sample by a laser beam passed through a microscope, spectral lines of elements in the rising vapor are photographed and evaluated quantitatively by optical scanning methods.

The procedure is shedding new light on the relationship of zinc to cirrhosis and cancer, cadmium to kidney disease, selenium to muscle metabolism, and aluminum to diseases of the lung—all part of the general problem of toxicity of common metals.

Another biomedical engineering achievement in fiscal year 1968 was the development of a new instrument that continuously tells a physician whether proper lung function is being maintained in critically ill or injured patients. It is a small, wristwatch-like sensor which detects subtle danger signals in breathing patterns by measuring automatically, through the intact skin, the amount of carbon dioxide in a patient's blood stream. Institute supported physicians and engineers who developed the sensor believe it will help reduce substantially the number of Americans who die each year from acute respiratory disorders, including 20,000 infants who die in the first 5 days of life from an occult breathing disorder known as acute respiratory syndrome, and more than 17,000 patients who die from emphysema.

TRAUMA

The goal of the Institute's trauma research program is to discover or improve lifesaving techniques for treating severely injured persons. Trauma often is termed the "neglected disease" of our society. Epidemic in scope, it is the leading cause of death in the first half of the life span. For every person killed, a dozen or more are hospitalized. These patients now require 22 million bed days a year, or 12 percent of all available hospital space. Injuries cost the Nation's economy nearly $20 billion annually, exclusive of the human suffering and social disruption which attends them.

Except for work carried out by the military services, efforts to control and reduce loss of life from injuries (100,000 deaths per year) has centered largely on measures to prevent accidents.

Substantial gains can be made by a concerted effort to understand and counter the succession of barely perceived physiological changes and events which attend and often precipitate death following severe injury.

To this end, a major Institute program stimulates and supports development of university-based centers for trauma research. These centers combine high quality clinical and emergency treatment facilities with interrelated research by scientists in a number of disciplines. The goal is to define patient problems, test findings in the laboratory, and apply solutions to patient care at the earliest possible moment.

Four trauma research centers were established this year. One, at the University of Cincinnati, Cincinnati, Ohio, is concentrating on the problem of infections resulting from trauma. A second center, at Parkland Memorial Hospital in Dallas, Tex., is concerned with causes and ways to correct kidney failure, loss of fluid balance, reduced heart function, circulatory disturbances, respiratory distress and other life-threatening factors. The other two new centers are located at Albany Medical College, Albany, N.Y., and the University of Maryland, Baltimore, Md.

Although the Institute's program is relatively new, important information has been gained. New methods to measure and evaluate body fluid balance have been discovered. Imbalances in body fluid often occur with patients who have undergone severe shock as, for example, when the skin vapor barrier is destroyed by severe burns or when there is massive destruction of tissue. Early and precise measurement of these imbalances is essential to successful therapy.

Also, a new topical antibacterial agent which has been synthesized has proved highly effective in controlling infection in burn wounds. Studies of endotoxin shock, caused also by bacteria, have produced new methods for treatment which in animals have reduced the fatality rate by 20 percent.

RESEARCH TRAINING

Institute research training grants and fellowship awards this year supported more than 7,500 young men and women of unusual promise in universities throughout the country. In fundamental health sciences alone, Institute support provides training for about 40 percent of the total national graduate enrollment. In some disciplines, this figure is as high as 70 percent.

This support has a substantial impact on the future quality of medical education. Past experience has demonstrated that half of all Institute-supported trainees and fellows are recruited for research and academic positions in the Nation's medical schools. Ph. D. candidates receiving Institute support tend to complete their studies more than a year earlier than those who do not receive such assistance.

National Institute of Neurological Diseases and Blindness

In the 15 years of its existence, the National Institute of Neurological Diseases and Blindness (NINDB) has developed a broad program of basic and applied research both at its Bethesda, Md., laboratories and at grantee institutions. It has strengthened this program by training scientists to cope with the complexities of neurological research.

Prime targets during the past year included cerebrovascular disease (strokes), epilepsy, degenerative neurological disorders, problems associated with head injury, disorders of vision, and the events of the perinatal period which may cause conditions such as cerebral palsy and mental retardation.

COLLABORATIVE PERINATAL PROJECT

The most critical time of life is the period from conception to shortly after birth. Often marked by excessive fetal loss and infant mortality, this perinatal period is also the source of many neurological disorders and of a large percentage of mental retardation. Scientists of the Institute gained greater insight this year into the importance of the prenatal period in total development. Scientists in the Institute's collaborative perinatal project found strong evidence that malnutrition in a pregnant woman adversely affects the intelligence of her child. They believe the impairment can result either from an inadequate food supply of proteins and calories or from a chemical nutritional imbalance traceable to disease.

Mild depression of intellect occurs more frequently among the disadvantaged populations of this and other countries than among the privileged. Part of the difference of IQ between higher and lower socio-economic groups may be attributed to poor nutrition. If this line of thinking is substantiated by further investigations, a whole new approach to an age-old problem may be in the offing.

One of the most prevalent neurological disorders caused by unknown events during the perinatal period is cerebral palsy. Another study this year has confirmed previous work which indicated that spastic diplegia is a specific type of cerebral palsy found among premature infants. A survey of all premature births in the project, surviving to the age of one year and weighing less than 2,000 grams (about 4½ pounds), led investigators to confirm that almost all cerebral palsy cases classified as spastic diplegia occur in this weight group.

The Institute is intensively investigating many of the factors believed related to the causes of cerebral palsy at its Laboratory of Perinatal Physiology in Puerto Rico. Using the rhesus monkey as the experimental animal, scientists there are investigating such major problems as the role of asphyxia in brain damage, placental blood flow, placental insufficiency, and placental abruption. These are known complications in humans linked with infant death and high prematurity rate.

Scientists in the Puerto Rico laboratory found that the brain may not be as vulnerable to loss of oxygen for short periods as now commonly believed. It was found that the sudden production of total circulatory arrest is tolerated by the animal for up to 16 minutes without brain damage. Apparently less extreme but continued impairment of blood supply is the more common cause of the usual forms of cerebral palsy.

EPILEPSY RESEARCH

Epilepsy is another condition occurring early in life. Affecting a large number of people in the United States, epilepsy has been a major emphasis of the Institute's research program since its founding.

The major attack on epilepsy is being carried out through clinical research centers, established by NINDB in universities. These investigators are studying basic electrical activity of the brain, the way in which it can be surgically altered to reduce epileptic seizures, effects of drug therapy, and the basic mechanisms of epileptic discharges in animals. A pioneer computer laboratory is producing new information about the essential nature of the electrical nerve discharge.

Recognizing the need for better communication of research knowledge in epilepsy, the Institute has developed a new service, *Epilepsy Abstracts*. Each monthly issue digests approximately 200 articles related to epilepsy from the world's biomedical literature.

DISORDERS AFFECTING THE AGED

At the other end of the long scale of human development are disorders that affect the aged. These include stroke, Parkinson's disease, and many other neurological and sensory disorders.

New hope for sufferers of Parkinson's disease has been raised by the recent discovery of a possible new therapy. As a result of limited clinical trials, scientists now have evidence that L–DOPA, a synthetic amino acid that leads to the formation of dopamine in the brain, is effective in relieving the symptoms of parkinsonism in some cases. Whether these encouraging results presage a therapeutic breakthrough in parkinsonism remains to be seen.

A second condition which also largely affects the aged is cerebrovascular disease, or stroke. Stroke is one of the major targeted areas of the Institute. In addition to an extensive program of research projects in this area, 18 cerebrovascular research centers are now being supported in major population centers of the country. Each center is concentrating on a major approach to the disease problem. Factors being studied are the dynamics of cerebral blood flow, the biochemistry of blood constituents, the effect of anticoagulant drugs, cerebral cellular metabolism, and aphasia.

SCLEROSING DISORDERS

Another group of diseases or conditions which affect people mainly in their middle and most productive years are the sclerosing disorders. Multiple sclerosis (MS), the most common disease of this group, is a disease of temperate climates. A worldwide epidemiologic survey has revealed that the place where one spends early childhood is a determining factor in whether MS develops in later life. A study is now being planned to determine the latency of this disease and the most common age at which it is actually acquired.

Among the most dramatic developments highlighting the area of clinical investigation have been those relating to the role of unusual viral-like agents in degenerative disorders of the nervous system. The role of such an agent in kuru, a rare neurological disease found only in New Guinea, has now been well established. The role of a viral agent in subacute sclerosing panencephalitis has been virtually proven. There are indications that an atypical or incomplete form of measles virus is responsible for this disease, now found to be much more prevalent than previously recognized. These findings have wide implications for other chronic neurological disorders.

NEUROMUSCULAR DISEASES

A large group of disorders, the neuromuscular diseases, especially affect children and young people. These include muscular dystrophy (MD) in its various forms, myasthenia gravis (MG), and a number of less prevalent conditions.

Knowledge of the fundamental mechanism in myasthenia gravis is progressing rapidly. The disease is clearly related to abnormalities of the thymus gland. Institute studies now show that thymectomy is a useful procedure, especially in young women. The use of anticholinesterase drugs is increasingly effective. Germine diacetate has been found effective in treating MG patients who cannot be helped with anticholinesterase medication.

The specific metabolic defect present in each of three inherited, retarding, and progressively fatal disorders of infancy—in Niemann-Pick, Gaucher's, and Fabry's diseases—has been identified by Institute researchers, and blood tests developed to detect these diseases.

HEAD INJURY RESEARCH

Many of the estimated 10 percent of the population who suffer from some neurological condition are victims of accidents and have suffered head and spinal cord injury.

The Institute is conducting a laboratory program for head injury directed toward understanding the factors causing brain swelling after head injury. It has been proved this year that whiplash injuries, even without direct impact to the head, may cause brain concussion and bleeding. Experimental whiplash injury in rhesus monkeys has demonstrated that cerebral concussion, bleeding and contusions can be produced by rotational jarring of the head on the neck alone, without direct head impact.

RESEARCH ON SENSORY SYSTEMS

To the physician, the eye is one of the most valuable sources of information for diagnosis of systemic disease. By examining the back of the eye, he can learn a great deal about other diseases of the brain and its blood vessels. To improve the precision of such an examination, the Institute is developing a special television camera that can observe and measure subtle changes in the minute structures of the eye.

EYE RESEARCH PROGRAM

The Institute's eye research program is largely concentrated in 12 large clinical research centers. Research in these centers has recently produced notable advances in the successful repair of retinal detachment by better techniques of examination, surgery, and care. The laser has been used successfully to "spot weld" the retina in certain types of retinal detachment. The successful treatment of some patients with diabetic retinopathy has been accomplished by the removal of the pituitary gland.

Other advances include better diagnosis and treatment of glaucoma, more effective grafting of corneal transplants, tests to detect the harmful side effects of such drugs as chloroquine, and new methods of detecting and treating ocular tumors. A new drug, isosorbide, has been found to be a useful agent in acute primary and secondary glaucoma, and as a preoperative medication for various types of eye surgery.

The significance of advances of fundamental knowledge in vision research was highlighted this year when two of the Institute's grantees received Nobel Prizes for their contributions—Dr. Halden Keffer Hartline for studies of the physiology of vision, and Dr. George Wald for contributions to the understanding of the chemistry of the visual pigments.

INFORMATION NETWORK

To hasten dissemination of scientific information and to aid in program analysis, the Institute this year established a National Informaton Center on Vision Research at the Harvard University library. Objectives of the center are to define, identify, and store for retrieval the literature of vision so that the information may be more useful to research scientists, teachers, and practitioners. The vision center is the last of four such centers comprising the Institute's Information Network. This network is now providing scientific information to scientists through the world, covering basic and clinical neurology areas and communication.

Clinical Center

The Clinical Center provides necessary facilities and support services for the clinical investigation programs of the various NIH Institutes through its 516-bed research hospital. Primary consideration, however, is the welfare of the individual patient.

During fiscal year 1968, Clinical Center patients numbered 6,510. Readmitted patients outnumbered almost 2 to 1 those admitted for the first time. First registrations were 1,378; readmissions, 2,649. Outpatient registrations totaled 2,483. There were 4,027 patients admitted. Patients (adult and pediatric) were hospitalized for an average of 33 days; 69 percent of the beds were occupied on the average.

Construction of two additional floors (sixth and seventh) on the D wing was completed. The new area totals approximately 14,000 square feet. Occupancy by patient care staff took place in June.

In its first full year of operation, the Department of Nuclear Medicine conducted 3,246 complete studies and performed more than 1,300 laboratory and other surveys.

Television engineering was increasingly used in various diagnostic techniques. Installation of two new video tape recorders enabled the staff to completely tape biplane procedures from the Heart Catheterization Laboratory and images produced by the Nuclear Medicine Department's gamma scintillation camera.

More effective utilization of blood by the blood bank permitted 20,962 transfusions of blood or components from total acquisitions of 16,308 pints.

Clinical Pathology staff members worked with Bureau of Standards personnel on development and use of highly purified chemicals as standard materials for clinical chemistry. Notable progress was made on instrumental design for automated urine analyses.

Division of Biologics Standards

The Division of Biologics Standards (DBS) is responsible for administration of those provisions of the Public Health Service Act concerned with the Federal licensing and control of biologic products that are offered for sale in interstate commerce or for export or import.

These biologics include the vaccines, serums, toxins, antitoxins, as well as human blood and its derivatives, that are used for the prevention and treatment of diseases in man.

RUBELLA VACCINE

In the past several years, great strides have been made in rubella research. Infections of this disease during early pregnancy frequently result in spontaneous abortions, stillbirths, or birth of infants with grave defects such as blindness, deafness, heart disease, and brain damage. It has been estimated that during the last epidemic in the United States (1964–65), rubella led to 30,000 fetal deaths and the birth of 20,000 deformed children.

In 1966 two DBS scientists reported the attenuation or "taming" of the virus. They used their weakened virus (named HPV–77) to prepare the first effective experimental rubella vaccine. The HPV–77 strain was made freely available to investigators and pharmaceutical manufacturers here and abroad.

Vaccines prepared from this strain had been administered to approximately 20,000 persons by June 30, 1968. No vaccinees have experienced adverse reactions from the vaccine, and more than 90 percent have developed antibodies indicating immunity. Continued evaluation of the first children inoculated 2 years ago by the DBS team indicates that the level of vaccine-induced protective antibodies in their blood is unchanged. These observations encourage investigators to feel that the immunity conferred by the HPV–77 attenuated strain will be of long duration. Trials with HPV–77 vaccines have been conducted in the United States, Canada, England, France, Russia, Holland, Finland, Sweden, and Taiwan.

Studies have shown that the attenuated HPV–77 strain does not spread to contacts of vaccinees, such as other family members or, in institutional settings, other infants, children or young adults.

This past year, a simple blood test (HI test) to determine rubella immunity was perfected by DBS scientists. This procedure has now moved from the DBS research laboratory to international application in vaccine development centers, hospitals, diagnostic laboratories, and doctors' offices.

In vaccine work, the HI test is used to identify appropriate candidates (persons susceptible to rubella) for vaccine studies and to determine the antibody (immunity) response induced by the vaccines. Because of its simplicity, precision, and speed, the HI test is expected to advance the target date of a final rubella vaccine by about 1 year, and to result in a saving of over a million dollars in Government expenditures for rubella vaccine research.

RH$_0$ (D) IMMUNE GLOBULIN

Each year, about 300,000 babies whose mothers have Rh-negative blood and whose fathers have Rh-positive, are possible victims of Rh disease (erythroblastosis fetalis). It occurs in about 10 percent of all pregnancies in which an Rh-negative mother gives birth to an Rh-positive baby, and is estimated to cause the death of 5,000 infants in this country annually.

Rh incompatibility becomes a problem when, during birth, red blood cells pass from the fetus into the mother's blood stream. If the baby's cells have the Rh-positive factor, the Rh-negative mother's body may begin to develop antibodies against them, just as though it had been invaded by an infectious disease. The first child of an Rh-incompatible union is rarely affected, but serves to sensitize the mother so that, in future pregnancies, the sensitized mother's antibodies may enter the Rh-positive baby's blood stream and destroy the red cells.

The principal therapy for affected infants has been exchange blood transfusion, but for the past 8 years scientists in this country and abroad have been looking for a practical means of preventing the disease. After 12 months of intensive study, the DBS developed standards for Rh_o (D) immune globulin, a form of gamma globulin used to prevent Rh disease. This product, under the trade name of Rh_oGAM, was licensed in April 1968.

MULTIPLE ANTIGENS

DBS research on biological products is necessarily related to current public health and medical practice. Because of the many diseases which can be prevented by immunization, there has been a growing tendency to use multiple vaccines combined in one injection. The usefulness of multiple antigens, however, must be determined on the basis of the combined effect, and with the assurance that no component inhibits the immunogenic effect of another.

DBS scientists have pioneered over the past several years in investigating the possibility of combining certain live virus vaccines. In their early work (Upper Volta, West Africa 1964) they found that combined measles, smallpox, and yellow fever vaccines could be administered safely and effectively by jet inoculation into susceptible children. Such combinations are especially useful for mass immunization campaigns in the developing countries of the world.

Based in part on these early findings of DBS, one of the larger pharmaceutical manufacturers began developmental work on the combination of live measles and smallpox vaccines for commercial production. This cooperative effort resulted in the licensing in late 1967 of a combined measles-smallpox vaccine, the first commercial combination of live virus vaccines. It is anticipated that additional multiple antigens will be developed, and DBS research in this area is continuing on that premise.

MUMPS VACCINE

A live mumps vaccine, under extensive testing for safety and potency in DBS laboratories for a year and a half, was licensed in December 1967 for commercial distribution. The new, single-injection live vaccine, which was developed by the manufacturer over a 5-year period, is prepared in chick embryo culture—the system which is already in use for the production of live measles vaccines. In the nationwide clinical tests, approximately 95 percent of the susceptible children and adults to whom it was administered developed protective antibodies.

The vaccine is recommended for children approaching puberty, adolescents, and adults who have not had mumps. It is not recommended for younger children pending development of more information on the duration of immunity. Mumps infects about 80 percent of the population before adulthood and is usually regarded as an innocuous disease in childhood, although complications may occur. After the onset of puberty, however, the virus may affect the reproductive organs.

INFLUENZA VACCINES

Influenza vaccine was first licensed in 1945. Unlike vaccines against other virus diseases, the protection provided by influenza vaccines depends on representation of prevalent virus strains known to have caused recent influenza epidemics. The properties of these viruses do not remain constant but change from time to time in unpredictable ways.

Since influenza has a worldwide incidence, DBS keeps in close contact with influenza centers throughout the world. A yearly review of epidemiologic and laboratory data obtained from many sources on the prevalent influenza viruses enables DBS to establish a vaccine formula suitable for the next year's influenza season.

Early in the spring of 1967, all influenza vaccine manufacturers were advised by the DBS of the desirability of making available two influenza vaccine formulas for the 1967–68 season: a newly introduced bivalent vaccine and the traditional polyvalent vaccine. The bivalent provides greater protection against current strains of influenza, whereas the polyvalent vaccine stimulates a broader immunologic response. Both the bivalent and the polyvalent vaccine formulas contain the same total quantity of influenza antigens, but the bivalent includes considerably greater representation of contemporary A_2 and B strains than is possible in the polyvalent.

Division of Computer Research and Technology

The Division of Computer Research and Technology is charged with planning and conducting research, developmental and demonstration programs in mathematical and other computer-related sciences, including information processing, in support of NIH programs. The Division provides a technical advisory resource in relevant areas of mathematics and other computer related sciences.

UTILIZATION OF ELECTRONIC DIGITAL COMPUTERS

During fiscal year 1968 conversion of the central computer facility to OS/360 equipment was achieved. A third 360/50 was installed May 1968, and significant advancements were made in modifying the vendor-supplied operating system to provide reliable, efficient and responsive machine servicing to the broad computer needs of NIH. Computational and programming support to research and management programs was increased.

In fiscal year 1968 the Division took initial steps in establishing a computer center to handle all computer needs and requirements of the Institutes and Divisions. Currently, the center has approximately 700 users. Ultimately it will enable any NIH scientist to type out in program language a request for information, send it to the center via telephone lines, and promptly receive the required information.

Two projects, both of which will increase computer efficiency while resulting in reduction of costs, were initiated. One project involved implementation of two systems—HASP and SPOUT—on the 360/50 computers, and increased computer throughput by about 30 percent while realizing an estimated savings of $30,000 in fiscal year 1968. The two systems, operating in defined segments of the computer's memory at the same time, increased the total of jobs processed per day from 350 in January 1968 to well over 600 per day in May.

A shared libraries project involved establishing a central library for programs which all Division computers may use, which is expected to significantly reduce costs.

OTHER PROGRAM ACHIEVEMENTS

A 360 program for adaptive filtering of bioelectric signals was completed and documented, and supplementary methods of programming were developed by the Laboratory of Applied Studies. This technique permits analysis of noise patterns in relation to signal content, and estimating of signal/noise ratios in many experimental situations. A system of linked computer programs completed in fiscal year 1968 made it possible to analyze continuously recorded measurements of cardiac pressures and blood flow obtained during heart surgery and diagnostic procedures.

In the Laboratory of Physical Sciences, numerical procedures and programs were developed for interpreting nuclear magnetic resonance data. A mathematical model was developed for the effects of noise on nerves.

The Heuristics Laboratory was established in midyear to develop concepts, techniques, and programs for automatic answering of questions and deductive solving of biomedical problems.

A major effort by the Computation and Data Processing Branch molded the vendor-supplied IBM 360 software into a reliable, responsive, and expandable computer system. Computers are now able to operate with four simultaneous streams. While computation of one program is underway, input for the next few jobs is simultaneously being read in and stored. Results for the last several jobs are being printed simultaneously, with one output stream and one printer devoted to systems messages, diagnostics, and small scientific results that have immediate relevance, and another output stream and printer to large printing loads resulting from administrative and management data processing.

Tablemaker II became operational on new hardware early in the year. This device enables anyone with no computer experience to take a basic file of data, extract relevant information, recode the control variables or otherwise regroup or reexpress the data. The data can be operated on by logical or arithmetic operations to computer frequencies, averages or expectancy tables, and then presented along with appropriate descriptive material in tabular form.

Division of Environmental Health Sciences

The mission of the Division of Environmental Health Sciences is to determine the significance and magnitude of the health hazard of low-level concentrations of biological, chemical, and physical agents present in or introduced into our environment. The Division tests selected contaminants, singly and in combination, to determine the underlying mechanisms of adverse response, with the goal of determining standards and guidelines for protective or preventive control measures.

CONSULTATIVE SERVICES

During the year, the Division provided consultative services, guidance, and documents for the following environmental problems to other Federal agencies:

- Lung-cancer hazards to uranium miners.
- Hazards associated with the asbestosis problem.
- Position documents on smoking and health.
- Pesticide hazards to man including DDT, DDD, and DDE in milk and milk products.
- Potential hazards of Mace as a riot-control agent.
- Problems of drinking-water quality standards and the water recycling program.
- Carcinogenic hazards associated with particulate contamination of the air.

LABORATORY RESEARCH

During this fiscal year, an in-house laboratory research program was launched at the National Environmental Health Sciences Center (NEHSC), the intramural research component of the Division.

ANIMAL SCIENCE AND TECHNOLOGY

The Animal Science and Technology Branch, during the year, conducted research in the following areas: interactions between chemicals, such as heavy metal salts and pesticides, and viral infections; the effect of a prototype alkylating agent on the immune responses of rabbits to an attenuated viral vaccine; the effect of whole body gamma radiation on the immune response of rabbits to an attenuated viral vaccine; a project to test the suitability of hydroponically grown grass as a supplement for laboratory animal diets; and a study of embryo development as a measure of environmental changes.

CELL BIOLOGY

Research programs being carried out by Cell Biology Branch scientists included: studies on toxin production by fungi found on vegetables and other foodstuffs for human consumption; studies of the effects of compounds, such as pesticides and heavy metals, on enzymatic and other processes involved in collagen synthesis and differentiation of cells and tissues; studies on the effects of selected alkylating agents in inflammatory reactions, on the synthesis and functioning of peptide hormones, and on specific enzymes and metabolic processes; and studies on the effects of pesticides and other environmental toxicants on cell membrane structure and function.

PHARMACOLOGY AND TOXICOLOGY

Pharmacology and Toxicology Branch research was designed to study the chronic effects of long-term, low-level exposures to environmental agents. Projects centered on such areas as: the influence certain compounds which pass the placental barrier have upon the fetus; teratogenic responses to administration of specific drugs; the postnatal effects of prenatally administered chemicals on the developing fetus; and genetically determined characteristics that modify response to chemicals.

ANALYTICAL AND SYNTHETIC CHEMISTRY

Accomplishments of the Chemistry Branch included: the assembly of environmental chambers for the elaboration of the effects of ultraviolet radiation, ozone exposure, and other factors on the stability of certain groups of pesticides; the separation and identification of components of oils of calamus and nutmeg by chromatographic and spectroscopic techniques; and the synthesis of intermediates for metabolic and teratogenic studies.

OCCUPATIONAL STUDIES

The Occupational Studies Program continued and completed several studies transferred from the National Cancer Institute in July 1967: Also, an analysis of uranium miner data led to a report to the Federal Radiation Council for a review of radiation exposure in miners; assessment of steelworker mortality findings; updating of mortality findings on chromate paint workers; and assessment of data on other industrial workers, such as those in the cutting oil industries.

RESEARCH PROJECT GRANTS

The increasing use of soaps, cosmetics, detergents, antibiotics, diuretics, and tranquilizers containing photochemical agents is multiplying the number of patients experiencing externally induced skin diseases. Grantees of the Division have developed a phototesting unit that facilitates the development of screening tests for the prediction of the photoactivity of chemicals prior to their commercial use.

Although satisfactory procedures for the detection of pesticides in fat tissue have been available for some time, these methods are not sufficiently sensitive to detect these pesticides in tissues such as liver, brain, gonad, and kidney in the minute concentrations in which they are present in the general population. A group of grantees has developed a rapid, reliable procedure capable of detecting pesticides in concentrations of a fraction of a part per billion. This highly sensitive chemical procedure was then utilized in an attempt to discern current levels of exposure to pesticides in the general population as well as the occupationally exposed.

The role of the home usage of pesticides in the variable concentrations of pesticides stored in human bodies has been investigated by DEHS grantees. A striking correlation was observed between the concentration of the insecticide DDT and the degree of household exposure. The average DDT concentration in a group of people associated with high household usage of the insecticide was over four times the average concentration among individuals who rarely used pesticides in the home. The results suggest that while an average baseline concentration may be produced by pesticide-contaminated food, the household use of pesticides is responsible for increased pesticide levels in the body.

Swedish observations that heredity is an important factor in certain coronary and respiratory symptoms in smokers have been confirmed by Division grantees. A questionnaire addressed to almost 15,000 male twins sought information concerning medical data, smoking, and occupational activities. The lack of difference in the prevalence of coronary symptoms between smoking and nonsmoking twins suggests the importance of genetic factors in the development of coronary symptoms. Respiratory symptoms were more prevalent among smoking twins than among their nonsmoking counterparts, although the difference was not as marked as that found between smokers and nonsmokers in the general population. These findings indicate that both genetic factors and smoking influence the onset of respiratory symptoms.

The continuing release of new chemicals into the environment as a consequence of technological progress results in new and potentially hazardous exposures to human populations. Inasmuch as certain of these chemicals are accumulated in body tissues, the question is raised concerning the role these stored agents may play in interference with biological mechanisms and in development or exaggeration of chronic disease. A group of DEHS grantees has developed a method of measuring the concentrations of zinc, copper, cadmium, and lead in hair. A study of over 200 individuals of various ages in an urban population sample revealed gradual but varying increases in the metals over a lifespan. Inasmuch as cadmium tends to localize in such organs as the liver and kidney and to displace zinc, which is essential in trace amounts in certain cellular functions, further study is indicated concerning the role of long-term exposure to cadmium in human health.

Table 6.—*Division of Environmental Health Sciences, distribution of appropriation*

[In thousands]

	1967 actual	1968 actual
Research grants:		
Regular program:		
Noncompeting	$1,654	$3,631
Competing	896	360
Supplemental	67	34
New	1,451	924
Total, regular	4,068	4,949
Special program:		
General research support		547
University-based centers	2,529	3,000
Total, special	2,529	3,547
Total, research grants	6,597	8,496
Fellowships	99	42
Training grants	3,693	3,763
Total grants	10,389	12,301
Laboratory and clinical research	1,113	2,825
Research contracts	(100)	(583)
Review and approval	270	302
Program direction	145	274
Management fund	434	1,006
Total, direct operations	1,962	4,407
Total	12,351	16,708

UNIVERSITY-BASED CENTERS

A considerable portion of the Division's resources has been devoted to the development and support of comprehensive university-based centers for research and research training in environmental health—with particular relevance to human health. These centers provide a focus for continuous problem definition, synthesis of existing knowledge, research stimulation and training, as well as a collaborative attack on a host of current and emerging research problems.

During the past year an additional center was created, bringing the total number to five. This new center at the Harvard University School of Public Health will emphasize studies of the biological effects of atmospheric pollution, pesticides and other food residues, and the effects of body burdens of radionuclides and other chemicals.

Table 7.—***Research grants program analysis***

	1968 Estimate
Toxicology	$2,167,000
Pesticides	2,098,000
Natural products	325,000
Synthetic organics	218,000
Heavy metals	174,000
Smoking and health	82,000
Subtotal, regular program	5,064,000
General research support grants	547,000
University-based centers	3,000,000
Total, research grants	8,611,000

Division of Research Facilities and Resources

The Division of Research Facilities and Resources seeks to expand and improve the Nation's institutional resources essential to biomedical research and scientific progress through five programs: special research resources; general clinical research centers; animal resources; general research support; and health research facilities.

SPECIAL RESEARCH RESOURCES

This program provides biomedical research institutions throughout the United States with the complex, highly specialized equipment needed for advanced research but too expensive for individual projects.

In the fiscal year 1968, through grants totaling $10 million, the program supported 50 specialized research resources, of which 41 were computer centers and six were analytic biochemistry instrumentation resources.

Computer centers funded by this program made possible high-speed memory storage and retrieval as well as the collection, processing, and analysis of data on a massive scale, permitting studies otherwise inconceivable. They also can continuously monitor and automatically modify certain types of research experiments.

For example, in a study at Washington University, St. Louis, Mo., a machine was taught to recognize abnormalities in heart rhythm, making it possible to collect and rapidly analyze data on the electrical behavior of the heart following myocardial infarction. Ultimately, it is hoped this will lead to devices to alert the physician to undesirable coronary events taking place.

Another intriguing and potentially powerful advancement in computer technology is the capability of the computer to "read" and respond to the user in a conversational mode. While full exploitation of this power is many years away, a Division-sponsored study at the University of California in Los Angeles, has enabled a user to request individual or grouped patient data, ask detailed questions about it, and perform statistical evaluations. He may also display and analyze chromosomal patterns at the console.

GENERAL CLINICAL RESEARCH CENTERS

This program is designed to translate laboratory findings into new diagnostic and treatment techniques which can more readily be brought to the patient. During the fiscal year, the program provided $30,443,000 to support 91 centers. New advances against disease and disability were made in many areas.

A group of hypertensive patients was found to have markedly increased production of certain adrenal hormones. It was found that these individuals have a specific adrenal enzyme defect which results in abnormally high rates of adrenocorticotropin (ACTH) production. In these patients, ACTH secretion has been suppressed by small doses of hydrocortisone, and lifelong hypertension has been cured.

Two centers have undertaken thymus transplants, one with notable success, in an attempt to reconstitute immunologic reactivity in patients with fatal deficiencies in this regard. In the successful case, a thymus gland from an aborted fetus was transplanted into an infant born without the gland. Since implantation, the baby has thrived and his blood counts are normal; he can reject a skin graft and has had no significant infections.

The diagnosis, treatment, and basic understanding of cancer continues to evoke massive research efforts at the centers. The site of many tumors can now be identified by an elevated temperature of the overlying skin, as heat is produced by the increased metabolic activity accompanying malignancy. Thermography is being utilized to discover previously unidentified foci of malignancy, especially in the breast, and to measure the effectiveness of various kinds of therapy.

A valuable adjunct of the clinical center program has been the training of medical students, interns, nurses, and other medical personnel. Reports for fiscal year 1967, the most recent year for which data is available, indicate that more than 5,000 medical students, interns, residents, and fellows have been trained through this program. Of this number, almost 2,000 were medical students.

ANIMAL RESOURCES

The animal resources program helps institutions secure the high-quality research animals needed for biomedical investigation. The program supported 58 animal resource projects under an appropriation of $5.1 million.

Established in 1967, the Reference Center for the Study of Primate Viruses, a national resource at the Southwest Foundation for Research and Education in San Antonio, Tex., provided such services as a working repository of newly isolated primate viruses, and an information exchange between primate centers and other research organizations using the baboon as a research model; it also served as a source of reference reagents for new and existing prototype viruses.

The Animal Resources Branch also awarded eight training grants totaling $318,000 in fiscal year 1968. Awarded to academic institutions to support postdoctoral training for veterinarians in laboratory animal medicine, these grants supported 26 trainees in programs requiring 2 to 3 years for completion. With an appropriation of $200,000, the laboratory animal science fellowship program offered approximately 20 postdoctoral and special fellowships to qualified individuals holding the D.V.M., M.D., or Ph. D. degree.

The seven regional primate research centers were instrumental in improving animal care and veterinary medicine for primates. In fiscal year 1968, $10.5 million was appropriated for this program.

Also during the year, 111 professional center core staff members were actively engaged in research at primate centers, which provided facilities and assistance for 32 visiting scientists and material for 83 collaborators from numerous domestic and foreign universities. The center core staff was engaged in 44 federally supported project grants totaling $2,532,000.

GENERAL RESEARCH SUPPORT

The general research support programs help institutions develop their scientific research capabilities so they may become effective partners with the Federal Government in the pursuit of the biomedical research and research training objectives important to both.

The program is composed of three distinct elements: general research support, biomedical sciences support, and health sciences advancement awards.

During fiscal year 1968, $48.2 million was distributed to 311 institutions for GRS support. Of this total, $25.8 million went to medical schools. The next largest category, hospitals, received $8.2 million.

At the University of Colorado School of Medicine, Denver, Colo., under this program, a screening test was devised for evaluating the intellectual and behavioral development of children from birth to 6 years. The test has proven so valuable that the American Academy of Pediatrics has recommended its routine use to pediatricians, and it has been adopted on a nationwide basis for evaluating Project Headstart children. Hundreds of requests about this test have been received by the Division from schools and pediatric organizations.

The biomedical sciences support grant program was initiated to include nonhealth professional components of the graduate divisions of academic institutions. In 1968, $7.5 million was appropriated for this program and awards were made to 102 institutions.

The health sciences advancement award program is a competitive program to encourage comprehensive institutional advancement toward excellence in biomedical research and research training. It provides grants to carefully selected colleges and universities that can become institutionally distinguished in research and research training by developing their facilities, staff, and research potential. The 1968 appropriation of $4 million permitted two new awards, bringing the total to nine.

HEALTH RESEARCH FACILITIES

The health research facilities construction program, created in 1956 to expand the Nation's physical facilities for research in the health sciences, supports grants for new construction and remodeling of present facilities. In fiscal year 1968, 45 grants totaling $39,482,293 were awarded; 40 facilities employing construction grant funds were completed.

Exciting work in cardiovascular surgery, pioneered by distinguished investigators such as Drs. Michael DeBakey, Adrian Kantrowitz, and Norman Shumway, has been performed in facilities funded partly by grants from the health research facilities program. Similarly, Drs. Arthur Kornberg and M. Goulian did their epoch-making work on the synthesis of DNA—popularly described as the creation of living matter in the test tube—in facilities built with the assistance of health research facilities program funds.

In the 12 years since its inception, the health research facilities program has awarded 1,462 grants totaling over $452 million. The 406 recipient institutions have contributed over $600 million in matching non-Federal funds to these moneys, resulting in the addition of over 18 million net square feet of space to the Nation's health research resources.

Division of Research Grants

At the beginning of fiscal year 1968, an office was established within the Office of the Director, DRG, to undertake responsibility for two "single-manner" functions delegated to the Division by the Surgeon General: (1) the evaluation of assurances received from grantee institutions in compliance with PHS policy on projects involving human subjects; and (2) the expansion of the program to authorize certain major PHS grantees to undertake increased management responsibility for prior approval changes in restricted budget categories.

In April 1968 the Division assumed responsibility for coordinating and issuing NIH extramural policy and procedural materials.

Throughout the period under review, the Division continued to receive and process research, research training, and research fellowship applications for all sectors of the Public Health Service. An estimated 30,000 grant and award applications were received by the Division. Of these, 25,003 research grant applications were processed and assigned of which 11,000 or more were reviewed for scientific merit by the DRG study sections and committees. The Division also received and assigned 5,097 new and competing renewal fellowship award applications; 530 new and competing renewal research career applications, and 2,165 new and competing renewal training grant applications.

There was an overall increase in training program applications of 4.5 percent in new and competing renewal, and 1.5 percent in all training applications received and assigned over the previous year.

More than 18,000 reprints and 2,000 progress reports resulting from PHS-supported research were received and distributed to appropriate offices and staff.

Division of Research Services

The Division of Research Services provides scientific, technical, and engineering services to support and further the research programs of the NIH.

The programs of the Division may be divided into two broad classifications: programs in direct support of research; and programs related to NIH facilities and proper environment.

The Division of Research Services is comprised of eight branches: Engineering Design; Construction Engineering; Plant Engineering;

Environmental Services; Biomedical Engineering and Instrumentation; Laboratory Aids; the NIH Library; and Medical Arts and Photography.

Recently the Division strengthened management of DRS activities by realining functions within and among several of the branches.

The most extensive area of reorganization concerns the former Research Facilities Planning Branch and the Plant Engineering Branch. To handle NIH's increased construction and maintenance workloads, RFPB was abolished and its elements regrouped into an Engineering Design Branch and a Construction Engineering Branch. At the same time, the engineering design and construction activities of PEB were transferred into the appropriate new branches, with PEB retaining responsibility for operation, maintenance, and alterations of the NIH buildings and grounds.

In another change, the sectional structure of the Environmental Services Branch was reorganized to enable the branch to be more responsive to Institute needs. The branch organization is now based on functional programs rather than professional disciplines, and recognizes the growing role of biohazards control as a prime factor in maintaining a satisfactory environment.

CONSTRUCTION

A primary function of DRS is administering NIH construction programs. In fiscal year 1968, design and construction associated with the expansion of NIH facilities continued at a record pace. The current program includes more than 20 projects in various stages of planning, design, or construction, having a total cost in excess of $100 million. Eleven projects were under construction during the year. The Gerontology Research Center, a 93,000-square-foot laboratory building located on the Baltimore City Hospital's grounds, was completed. Also, three major construction projects were carried to virtual completion during the year. The projects are the NCI virus isolation facility, located southwest of the National Library of Medicine, the library and cafeteria additions to the south side of the Clinical Center, and the 2-story addition to wing D, on the south side of the Clinical Center. The design of several projects, including two multilevel parking facilities, was nearly completed.

RESEARCH ANIMALS

DRS also provides research animals for NIH scientists. Over a million laboratory rodents and rabbits were produced in 1968. Major emphasis was placed upon data processing of production and animal issue information, to achieve greater efficiency in the utilization of limited production facilities.

Programs to improve the quality of all animals furnished to intramural research programs were continued. For the first year in recent history, the rodent and rabbit production colonies experienced no major outbreaks of disease. Significant improvement was made in the quality of the random source dogs and cats issued. This is directly attributable to the lengthening of the conditioning period from 30 to 45 days.

A development of singular importance, the successful establishment of a large colony of donor dogs to furnish whole blood, has resulted in a significant reduction in the number of dogs required for research purposes at NIH. The furnishing of blood, coupled with improvements in the health status of conditioned random source dogs, reduced the need for dogs by 786 animals. Projected dog issues for the year were 3,612, the fewest number of dogs issued since fiscal year 1960.

BIOMEDICAL ENGINEERING

A dramatic new area of research support in DRS is biomedical engineering, which combines the talents of engineers and medical researchers. Major emphasis was placed on direct collaboration between DRS professional staff and intramural researchers in the conduct of biomedical research and development programs.

The biomedical engineering staff was involved in approximately 400 research and development tasks. During the year, the staff made noteworthy original contributions in the areas of artificial organs, materials, laser technology, mechanization, automation, physiological monitoring, patient care, and physiological systems analysis.

NIH GRANTS AND AWARDS BY INSTITUTE OR DIVISION AND PROGRAM, FY 1968 [1]

(Dollars in millions)

Component	Total amount	Research grants [2]		Construction grants		Training grants		Fellowships [3]		Research career awards		Research contracts [4]	
		Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Total	$1,196.2	13,121	$626.4	109	$179.7	4,706	$237.5	3,798	$ 28.6	1,267	$ 26.8	1,088	$ 97.1
Research Institutes and Divisions	939.0	12,947	620.7	51	41.1	2,405	131.9	3,592	27.6	1,267	26.8	956	90.7
NIAID	71.9	1,411	49.0	—	—	187	8.8	148	1.4	122	2.5	146	10.2
NIAMD	112.5	2,503	85.5	—	—	325	15.3	306	3.0	161	3.6	66	5.1
NCI	127.9	1,335	71.6	—	—	209	11.1	211	1.9	98	2.2	364	41.2
NICHD	53.4	1,056	38.1	—	—	150	9.6	136	1.3	109	2.3	33	2.0
NIDR	21.7	339	14.3	—	—	114	5.2	77	0.8	51	1.0	21	0.5
NIEHS	12.0	100	7.9	—	—	51	3.7	6	(5)	—	—	5	0.3
NIGMS	141.2	1,576	74.1	—	—	650	44.4	2,014	12.4	378	7.7	28	2.5
NHI	133.1	2,123	94.9	—	—	402	17.3	194	2.0	214	4.8	144	14.2
NINDB	96.2	1,771	65.7	—	—	309	16.1	325	3.3	134	2.7	63	8.4
DRFR	159.7	635	117.1	51	41.1	8	0.4	16	0.1	—	—	10	1.0
DBS	1.5	—	—	—	—	—	—	—	—	—	—	28	1.5
DRS, DRG, DCRT	1.4	—	—	—	—	—	—	—	—	—	—	15	1.4
OD, CC joint	2.2	—	—	—	—	—	—	—	—	—	—	24	2.2
FIC	4.3	98	2.5	—	—	—	—	159	1.4	—	—	9	0.4
Bu. Health Prof. Educ. & Manpower Train	241.2	109	4.3	49	128.6	2,286	104.6	200	0.9	—	—	90	3.0
DAHPH	12.1	—	—	—	—	295	11.7	—	—	—	—	9	0.4
DDH	6.0	42	1.3	—	—	59	3.6	8	0.1	—	—	36	1.1
DHMES	66.9	—	—	—	—	1,009	66.5	77	0.3	—	—	2	0.1
DN	43.3	60	2.6	23	16.7	923	22.8	115	0.5	—	—	27	0.7
DPM	112.9	7	0.4	26	111.9	—	—	—	—	—	—	16	0.7
Nat. Lib. Med.	16.1	65	1.6	9	10.0	15	0.9	6	0.1	—	—	39	3.5

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[1] Excludes scientific evaluation grants as follows: research grants, $2.2 million; training grants, $0.7 million; and research career awards, $0.03 million.
[2] Includes general research support and research resources grants.
[3] Includes 279 traineeships for $2.6 million.
[4] Includes 3 contracts for $3,644 for the Bureau of Health Professions Education and Manpower Training, Office of Information.
[5] Less than $50,000.

NIH APPROPRIATIONS, FY 1968

(In thousands)

Activity	Total	General research & serv.	Allergy	Arthritis	Cancer	Child health	Dental
Total*	$1,566,749	$81,141	$94,422	$143,954	$183,356	$68,621	$30,307
Grants	890,186	68,262	66,454	118,601	98,993	56,795	23,349
Research grants	642,489	66,364	52,936	96,304	83,317	42,931	15,909
Regional medical programs	53,900	—	—	—	—	—	—
Research fellowships	54,991	1,580	4,267	6,591	4,326	4,102	1,971
Training grants	138,806	318	9,251	15,706	11,350	9,762	5,469
Direct operations	253,738	12,879	27,968	25,353	84,363	11,826	6,958
Direct research	81,165	—	13,746	14,333	16,065	5,742	4,598
Biometry & epidemiology	9,923	—	1,356	751	1,410	1,939	435
Collaborative studies	113,037	1,991	11,025	7,736	62,985	1,387	860
Biologics standards	8,649	—	—	—	—	—	—
Training	1,129	187	—	—	—	91	—
Prof. & tech. assist.	2,968	—	—	—	—	—	—
Review & approval	19,433	1,511	1,482	2,157	2,588	1,786	662
Program direction	8,887	1,143	359	376	1,315	881	403
International research**	3,872	3,872	—	—	—	—	—
Computer res. & tech.	4,675	4,675	—	—	—	—	—
Construction grants	35,000	—	—	—	—	—	—
Health Prof. Educ. & Manpower Training:	367,913	—	—	—	—	—	—
Health Manpower	164,663	—	—	—	—	—	—
Construction grants	203,000	—	—	—	—	—	—
Loan funds	250	—	—	—	—	—	—
National Library of Medicine	19,912	—	—	—	—	—	—

*Does not include direct construction or the special foreign currency program.

**Total includes $500,000 planning grant for construction of an international center, though separate column is not shown.

Envir. health sciences	General medical sciences	Heart	Neurology	Biologics stand-ards	Health research facilities	Regional medical programs	Bureau of Health Man-power etc.	Natl. Library of Med.
$17,289	$160,284	$167,954	$128,633	$8,649	$35,000	$58,814	$367,913	$19,912
13,166	151,902	131,763	107,001	—	—	53,900	—	—
8,421	85,263	106,628	84,416	—	—	—	—	—
—	—	—	—	—	—	53,900	—	—
—	20,910	7,439	3,805	—	—	—	—	—
4,745	45,729	17,696	18,780	—	—	—	—	—
4,123	8,382	36,191	21,632	8,649	—	4,914	—	—
3,549	—	13,135	9,997	—	—	—	—	—
—	—	1,727	2,305	—	—	—	—	—
—	3,547	17,526	5,980	—	—	—	—	—
—	—	—	—	8,649	—	—	—	—
—	484	295	72	—	—	—	—	—
—	—	—	—	—	—	2,968	—	—
356	3,023	2,663	2,389	—	—	816	—	—
218	1,328	845	889	—	—	1,130	—	—
—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—
—	—	—	—	—	35,000	—	—	—
—	—	—	—	—	—	—	367,913	—
—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	19,912

NIH EMPLOYMENT BY PROGRAM, JULY 1, 1967

	Full-time
Total	13,105
OD	1,434
Allergy	700
Arthritis	635
Cancer	1,441
Child Health	347
Dental	296
General Medical Sciences	199
Heart	661
Mental Health	—
Neurology	806
Clinical Center	1,600
Biologics Standards	302
Computer Res. & Tech.	274
Env. Health Sci.	60
Res. Facilities & Resources	144
Research Grants	565
Regional Medical Programs	95
Research Services	1,245
Bu. Health Manpower	851
Nat. Library of Medicine	522

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